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THE CASPER PROJECT—AN ENFORCED MASS-CULTURE STREPTOCOCCIC CONTROL PROGRAM

I. CLINICAL ASPECTS

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A program for reducing the incidence of streptococcic disease was instituted in a system of primary schools involving 6,460 children. All children with symptoms of respiratory infection were inspected daily; a culture was made from the nasopharynx of every child with signs of streptococcic infection; any child found infected with beta-hemolytic streptococci was excluded from school until antibiotic therapy had been started or (if such therapy was refused) until a negative culture was obtained. The program was found to be workable without any disruption of school routines. The cooperation of parents was excellent, and the project was financed without difficulty. On the basis of experience in the past, 18 and 27 new cases of rheumatic fever would have been expected for the school years 1955-1956 and 1956-1957 respectively; instead, only 3 and 2 cases were found. Enforced treatment or exclusion of school children infected with streptococci was found to be practicable. It was effective in reducing the incidence of rheumatic disease and valuable as a community educational effort.

INCRIMINATION of the group A beta-hemolytic streptococci in the genesis of rheumatic fever and nephritis has made it imperative that these organisms be detected and destroyed. While bacteriological culture and antibiotic therapy can accomplish these ends, practical application of these modalities on a mass basis has presented difficulties, economic and otherwise.[1] The "Wyoming Project" is an attempt to evolve workable methods of mass detection and treatment of hemolytic streptococci in school populations. This project began in Casper, Wyo., where an enforced mass-culture program for control of streptococcic disease has been under way in the entire primary school system (6,460 children) since 1954. The type of control program initiated here has since been launched in five other cities and towns, with results which will be reported later.

The program has been, in concept, simple. It has been built around three steps: (1) daily inspection of all school children presenting symptoms of upper respiratory infection, (2) culture of the nasopharynx in children manifesting one or more of the common signs of streptococcic infection, and (3) exclusion from school of all children found to be so infected until antibiotic therapy has been initiated or until a negative culture is obtained if such therapy is refused. Other projects of this general nature have been carried out, chiefly among members of the armed forces [2] and among some groups of school

From the Rheumatic Fever Control Committee. Dr. Phibbs is chairman of the committee, Dr. Becker is the pathologist at Natrona County Memorial Hospital, and Drs. Phibbs, Lowe, Fowler, and Scott are members of the Casper Clinic.

children.[3] The pioneer effort of Bunn and Bennett in Youngstown, Ohio, was the model for the Casper project. In the Youngstown study, the chief difficulty lay in the reluctance of the physicians to ad-

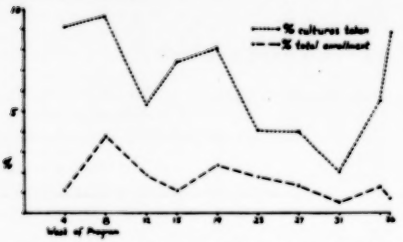

Fig. 1.—Incidence of positive cultures for beta-hemolytic streptococci in total grade school population (6,460 pupils) during 1956-1957. Detailed data are given in table 1.

minister adequate therapy once the streptococci had been detected—only 29% of the first 52 children found to be infected received proper treatment.

It was determined to remove this type of negligence from the realm of possibility in the Casper project. Streptococcic disease and its sequelae being the major public health problem in this area, strenuous efforts toward control appeared justified. To our knowledge, the Casper project is the only attempt to date to control streptococcic infection in an entire primary school population by classifying this type of infection as an excludable disease. The reasoning on which the program was based, together with the detailed organizational procedure, is outlined in part 2 of this study. In brief, large numbers of volunteer workers were trained to perform daily inspection of symptomatic children at each school, with throat cultures taken on suspicious individuals. Daily inspection and culture seemed essential since the time-lag involved in monthly or semimonthly cultures would allow rheumatic fever or nephritis to develop in the interim.

This program, it is emphasized, is an attempt to apply existing knowledge in actual prevention of the aforementioned diseases; it is not, except indirectly, a study of the epidemiology of streptococci. Primary school children were selected since they were the group most susceptible to rheumatic cardiac involvement [4] and since they represent, as well, an easily controlled segment.

Classification of streptococcic infection as a basis for exclusion from school is logically inescapable. It appears foolish to exclude children with such diseases as chickenpox, while permitting carriers of hemolytic streptococci to mingle with their schoolfellows. With the cooperation of the city-county health officer (Dr. R. P. Fitzgerald), and the ultimate authority of the state health department (under Dr. Franklin Yoder), this type of exclusion has been enforced without difficulty. All streptococci detected must be treated, whether the child is classed as a carrier or as diseased. In a program of this magnitude, determinations of antistreptolysin titers are out of the question; further, a carrier state in one child may produce active disease in any number of contacts.

As a compromise between safety and maintenance of school routine, infected children can reasonably be allowed to return to classes 24 hours after initiation of therapy.[1] The organism will not be completely eradicated, but the degree of infectiousness may be assumed to have dropped sharply—an idea which has been borne out by our own observations. (This, of course, does not apply to children in whom fever or other obvious, severe manifestations of streptococcic infection are present.) Children absent with respiratory infections are checked on return to school. The reader may note our emphasis on prevention of acute nephritis as well as rheumatic fever. Fulminating forms of hemorrhagic nephritis are fairly common in this region. We have been puzzled about the failure of other streptococcic-control projects to mention this feature. (Possibly the nonexistence of an American Kidney Association is a factor.)

Methods

For details of culture-taking, plating, and reporting, the reader is again referred to part 2 of the study. Standards of adequacy in therapy have con-

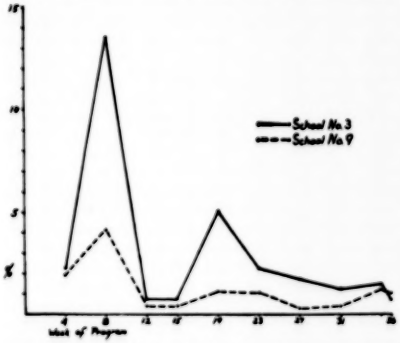

Fig. 2.—Incidence of positive cultures for beta-hemolytic streptococci in high-incidence and near-median incidence schools during 1956-1957. Figures are based on positive cultures per 100 students enrolled in each school during indicated periods. Detailed data are given in table 1.

formed to those recommended by the American Heart Association, i. e., 600,000 units of benzathine penicillin G intramuscularly, or three injections of 300,000 units of penicillin in aluminum monostearate, or 10 days' oral therapy with penicillin.

The goal of the program is a reduction in numbers of new cases of rheumatic fever and nephritis. This statistic is vital for purposes of evaluation. One member of the committee (R. H.) has been occupied with the task of locating and verifying new cases of either disease. The entire committee reviews each case of either disease to evaluate the diagnosis. Besides checking with physicians, the committee questions school and hospital nurses, teachers, and principals to make sure no cases go unreported.

Public information is a major preoccupation. Local newspapers and radio stations have given generously of their resources. In the early months of the program, the publicity was so effective that the committee was besieged by parents from schools not yet included demanding this type of protection for their children. Cooperation by the members of the Natrona County Medical Society has been the real touchstone of success. It is gratifying to be able to report that every one of the 40 members has participated vigorously and intelligently. This is a *sine qua non*—unless the physicians in a community are united in understanding and implementing control measures, no program can even be started.

Results

The results for the school year 1955 and 1956 have been described elsewhere.[5] They are almost exactly duplicated by the results for the year 1956 and 1957, which will be presented here in detail. The effect of such a control program can be figured on two bases: (1) effect on the number of streptococcic infections per unit of time, and (2) effect on the incidence of new cases of rheumatic fever and nephritis. Figure 1 illustrates two quantities in the effect on the number of streptococcic infection. First (and most important) is the actual number of positive cultures per month per 100 students enrolled in the entire primary school system. The second is the percentage of cultures taken which were positive. The first figure is the more significant; percentage of positive cultures to cultures taken will vary with the skill and discernment of the culture-takers.

The schools were brought into the program over a period of several weeks, and it was not until the first part of October that the whole school population was adequately covered. Note the peak at this time. There was a steady decline in level of streptococcic infection until the Christmas holidays intervened. This hiatus was followed by a "post-holiday" peak, which was again followed by a steady decline through the rest of the year until May, at which time a minor rise is noted. This last rise deserves a comment. The prolonged low-incidence period through March and April had produced some relaxation in effort. In some schools, cultures were being taken only three times a week by the end of April. During the first two weeks of May, local physicians reported an abrupt rise in streptococcic infection in adults, almost of epidemic proportions. Daily checks were reinstituted, and within two weeks the impact of the epidemic on the school population was apparent. The reapplication of control measures prevented any serious consequences. Note that the actual number of positive cultures rose slightly, while the percentage of positive cultures rose very sharply. (This latter phenomenon may also reflect increased skill on the part of volunteer workers after a year of culture-taking.)

Figures 2 and 3 depict the same quantities in two representative schools. School 3 is one of the "high incidence" schools (although not the highest), with a large population (400 children). School 9 is a school which represents, almost exactly, the median level of infection. It is also a large school (775 children) and, being the only parochial school in

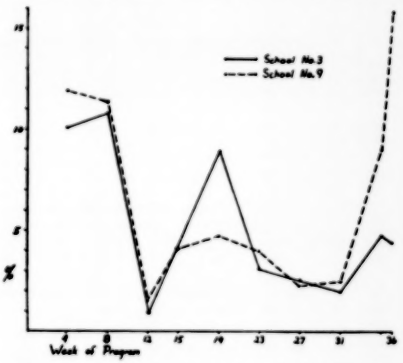

Fig. 3.—Incidence of positive cultures for beta-hemolytic streptococci in high-incidence and near-median incidence schools during 1956-1957. Figures based on positive cultures per 100 cultures taken during indicated periods. Detailed data are given in table 1.

the city, represents a widely scattered, diverse population. Figure 2, which again represents actual number of cultures per centum per month, shows the same phenomenon of high initial levels, a drop when the program is begun, a rise after holiday interruption, and a drop again on reinstitution of control measures. Table 1 presents the weekly figures for the total school system and for the two schools described. Note that in September and May, as well as over the Christmas holidays, allowance must be made for abbreviated school sessions.

To show variation in incidence, figure 4 represents the positive cultures per 100 students for the school year for each school. Note the wide spread in values. Streptococcic infections were found overwhelmingly concentrated in poorer economic levels

and areas. The same schools were in the high-incidence group in 1955-1956 and 1956-1957. The number of children with repeat positive cultures is indicated. Note that with few exceptions the number of schools with highest total incidence also had highest incidence of repeat positive infections. Table 2 presents these quantities in tabular form. In school 1, 45.7% of the children had at least one streptococcic infection during the school year. In school 15 only 2.2% of the children had one infection during the school year, while all variations between these two extremes are illustrated. One is struck with the danger of extrapolating from a small group or from studies conducted over a short period of time.

When a child was found repeatedly positive, or when siblings were found to be infected, the entire family was encouraged to report to the school for culture. One hundred one family groups were cultured in this manner—in 32 of these, one or more members of the family were found to be infected with beta-hemolytic streptococci (31%). Mass room cultures were performed at one school (no. 2) in an attempt to detect carriers. This afforded an opportunity to compare symptomatic with asymptomatic children. Three hundred forty-eight asymptomatic children had cultures done, with nine positive (2.6%). During the same period (11 days) 149 symptomatic children had cultures done, also with 9 positive (6%). This, of course, is a small

TABLE 1.—*Detailed Results of Cultures Obtained in High-Incidence School No. 3, Near-Median Incidence School No. 9, and All Schools During 1956-1957*

	All Schools (6,460)				School No. 3 (460)				School No. 9 (775)			
Week	No. Positive Cultures	No. Cultures Taken	% Positive of Total Enrollment	% Positive of Cultures Taken	No. Positive Cultures	No. Cultures Taken	% Positive of Total Enrollment	% Positive of Cultures Taken	No. Positive Cultures	No. Cultures Taken	% Positive of Total Enrollment	% Positive of Cultures Taken
9/16	5	45										
9/23	20	180							4	38		
9/30	31	390			5	61			2	47		
10/ 7	19	199			4	25			9	41		
Subtotal	75	823	1.16	9.12	9	86	2.25	10.1	15	126	1.94	11.9
10/14	70	618			23	149			13	90		
10/21	58	713			18	129			4	74		
10/28	31	440			5	130			3	50		
11/ 4	72	740			8	93			12	66		
Subtotal	243	2,511	3.76	9.68	54	501	13.5	10.8	32	280	4.13	11.4
11/11	47	625			1	68			1	67		
11/18	4	271			0	43			0	20		
11/25	32	708			1	113			0	59		
12/ 2	38	666			1	90			2	48		
Subtotal	121	2,270	1.88	5.33	3	314	0.75	0.96	3	194	0.39	1.55
12/ 9	47	598			2	48			2	47		
12/16	26	384			1	57			1	26		
12/23	0	0			0	0			0	0		
Subtotal	73	982	1.13	7.44	3	75	0.75	4.00	3	73	0.39	4.10
12/30	1	81			0	0			0	0		
1/ 6	38	634			9	64			5	68		
1/13	43	581			8	81			4	56		
1/20	50	560			3	79			0	65		
Subtotal	132	1,860	2.35	8.65	20	224	5.60	8.92	9	189	1.16	4.76
1/27	37	584			0	72			3	47		
2/ 3	78	694			5	54			2	48		
2/10	29	817			1	78			1	41		
2/17	32	750			3	77			2	60		
Subtotal	176	2,845	1.80	6.08	9	281	2.25	3.20	8	189	1.03	4.02
2/24	20	586			4	117			0	27		
3/ 3	29	577			1	62			2	28		
3/10	12	365			0	27			0	11		
3/17	28	650			2	57			0	22		
Subtotal	89	2,178	1.38	4.04	7	263	1.75	2.66	2	88	0.26	2.27
3/24	15	586			2	69			2	41		
3/31	7	508			0	73			0	27		
4/ 7	7	574			0	71			0	40		
4/14	10	250			0	31			1	11		
Subtotal	39	1,918	0.602	2.03	5	244	1.25	2.05	3	119	0.39	2.52
4/21	9	358			0	28			0	22		
4/28	13	360			1	39			2	31		
5/ 5	32	394			1	29			4	42		
5/12	29	346			4	35			6	37		
Subtotal	83	1,488	1.28	5.58	6	126	1.50	4.76	12	132	1.55	9.1
5/19	41	463	0.635	8.86	3	67	0.75	4.48	9	57	1.16	15.8

total group, and the results can only be classed as suggestive, even though the difference in terms of percentage is significant. The new cases of rheumatic fever per 1,000 children during the school year 1956-1957 was 0.3 in Casper with 6,460 children; 2.4 in Cheyenne with 5,769 children; and 4.1 in Laramie, Wyo., with 1,691 children. The new cases of glomerulonephritis per 1,000 children during the same time was none in Casper, 0.86 in Cheyenne, and 1.7 in Laramie. Unfortunately, reliable figures for previous years are not available.

Comment

Evaluation of a program of this type raises several questions. First, how effective is this program in detecting the presence of streptococci? By "this program" one must include the entire operation, starting with selection of children by teachers, inspection and culturing by volunteers, and laboratory processing. In other words, how effective is daily culturing of symptomatic children compared with periodic culturing of entire school populations? Other studies afford a comparison.

In the Youngstown study previously cited,[5] 6% of the children cultured were found to be infected with hemolytic streptococci. (These were children manifesting one or more of the signs of streptococcic infection.) Saslaw and Streitfeld, in an excellent study in Miami, Fla.,[6] reported incidences of isolation varying from 5.1 to 14.25%. These workers reported that 25 to 40% of 749 school children had at least one streptococcic infection per school year. This was a study in which mass cultures were performed periodically; no treatment was instituted. In a study currently underway in Riverton, Wyo.,[7] in which

TABLE 2.—*Incidence of Positive Cultures Obtained in Fifteen Schools During 1956-1957*

School, No.	Total Enrollment	Total Enrollment Positive, %	Individual Students Positive, %
1	118	62.0	45.7
2	539	33.7	25.4
3	400	29.9	22.7
4	358	24.0	17.9
5	302	21.0	19.3
6	146	18.5	15.1
7	543	13.0	10.7
8	716	12.5	11.5
9	775	12.4	10.4
10	579	11.8	10.2
11	101	10.0	9.9
12	710	9.8	8.5
13	446	9.1	7.7
14	330	7.3	7.3
15	497	2.2	2.2

throat swabs are plated immediately on blood agar, incidence of isolation has been in the neighborhood of 7 to 8%.

The values obtained in the Casper study were comparable to those cited above. One school (no. 1) showed a higher incidence of infection than any so far cited, to our knowledge. We have imposed the strict criterion of positive cultures per 100 students enrolled, since our program purposes control of all the students, by inspection as well as by culture. Most important, this is a program for treatment of streptococcic disease. Every infection discovered is treated. The drop in streptococcic infections which results inevitably alters figures for incidence. If the figures for the first month of the

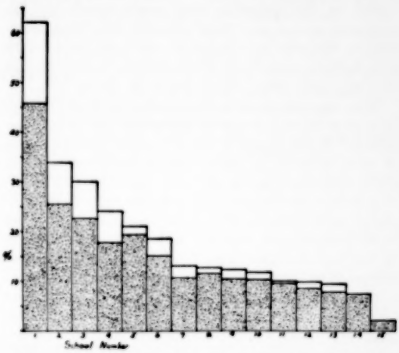

Fig. 4.—Schools arranged in [illegible] of incidence of positive cultures for beta-hemolytic strep[illegible]cci during 1956-1957. Figures based on number of positive cultures per 100 students enrolled in each school. Total height of each column represents total number of positive cultures obtained; stippled areas represent individual students with one or more positive cultures. The clear areas represent repeatedly positive cultures obtained during year. Detailed data are given in table 2.

program were extrapolated, the incidence of infection and of isolation would be a great deal higher than that found after months of enforced control. It is reasonable to conclude that the "Casper" type of project functions as efficiently in detecting streptococci as does periodic total-population culture.

Secondly, what effect does such a program have on the incidence of streptococcic disease? This has been answered in the results (fig. 1, 2, and 3). One can state simply that this type of control will predictably lower the incidence of streptococcic infection; one can state further that any interruption in control will be followed by a rise in incidence. A certain irreducible minimum of infection is inevitable, since the children are in contact with an uncontrolled population, but the control measures described appear to drop the level of infection to that minimum within a matter of weeks.

Third, are control figures available? A true control study was not possible. The actual throat swabbing was carried on by parents, and any attempt to refrain from treating a group of children would have met with understandable indignation.

Something like a control period evolved during the Christmas holidays. In almost every school, this two-week interruption was followed by a dramatic rise in incidence of streptococcic infection. Withdrawal of daily inspection and increased mingling with the uncontrolled population were probably the factors involved. This "post-holiday" rise subsided as the program was reinstituted, but its presence gave some idea of what the level of infection would be without the program. This phenomenon has been duplicated in other studies in Cheyenne, Wyo.," and Riverton, Wyo.[7]

How significant are the results in terms of appearance of new cases of rheumatic fever and nephritis? If one applied the 3% index, 18 new cases of rheumatic fever would have been expected in 1955-1956, and about 27 new cases in 1956-1957. We believe this is too high a figure, except for epidemic situations. Of the three new cases recorded in 1955-1956, one occurred in a child who was out of town at the time, and another in a boy who deliberately refrained from telling his teacher he had a sore throat because he "didn't want his throat swabbed." The total of two definite new cases in 1956-1957, with a third classed as "possible" by the committee, appears to be a low figure by any standards. No data at all are available as to incidence of nephritis per streptococcic infection, except for localized epidemic situations. Comparison with school populations in Cheyenne and Laramie revealed differences which seem impressive. The three communities are almost identical in climate, economic level, and degree of medical care available.

A significant number of cases of rheumatic fever are not preceded by any detectable respiratory infection. One can only hope that persistent daily treatment of all streptococci found will alter the total bacterial milieu so that the Streptococcus becomes a relatively rare organism, symptomatic or not. Our data appear to support this idea. Use of mass-culture methods have reduced the cost per culture (including subculture) to eight cents. Volunteer workers have performed the great part of the work, the only salaried employee being a part-time Heart Association nurse. As a result, the project can be financed without difficulty, and is planned to continue indefinitely. Since this point is crucial, detailed data in this regard are presented in part 2 of the study.

School routines are not disrupted. The total program at each school takes only a few minutes each morning. Teachers have unanimously affirmed a drop in absenteeism due to respiratory infection after institution of the project. All infections discovered can be treated. Some workers" have doubted this, fearing that treatment of all streptococci discovered might impose an impossible load. This has not been the case. Even in the high-incidence schools, all infected children have been treated with gratifying results. Except for isolated cases, the reaction of the parents has been that of grateful cooperation. In some areas, this has meant that about one out of every two school children has been treated at least once during the school year. This is a region in which the ravages of rheumatic fever and nephritis are all too familiar; parents will go to great lengths to avert either.

This program has proved a nonpareil in terms of spreading accurate information about rheumatic fever throughout the community. Previous efforts at lay and medical education had been, here as elsewhere, depressingly unrewarding. However, information about perennial prophylaxis was combined with talks to Parent-Teacher Association groups and training of volunteer workers in the present program, with astonishing effect. The fact that 20 or more mothers per school are thoroughly trained in the epidemiology of rheumatic fever and streptococcic infections assures the widest dissemination of this information. It is safe to say that there are few, if any, cases of rheumatic fever in this community which are not now maintained on antibiotic prophylaxis.

Summary

For three years, an enforced mass-culture program for detection and treatment of streptococcic disease has been under way in the primary schools of Casper, Wyo. The procedure consists of daily inspection of all "symptomatic" children with culture of suspicious individuals, and exclusion of those found to be infected with beta-hemolytic streptococci. Infected individuals are allowed to return to school only after adequate antibiotic therapy has been initiated. Introduction of this type of control produces a significant fall in incidence of streptococcic infection in the controlled population. Interruption of the program—as during the holidays—is followed by a rise in incidence of streptococcic infection. Reinstitution of control measures is followed by another drop in incidence. Family follow-up in cases of repeated infection discloses carriers in the family in 31% of the families studied.

In a small group of children (497) the incidence of streptococcic infection in symptomatic individuals was found to be significantly higher than in those who were asymptomatic. However, the group studied in this connection was too small to permit definite conclusions to be drawn. Enforced treatment or exclusion of school children infected with streptococci is both practicable and consistent with policy on other infectious diseases. This type of program appears to lower the incidence of new cases of rheumatic fever in the controlled groups to a highly significant degree. It seems likely that this program has been effective in lowering the incidence of new cases of acute nephritis in the controlled group. As an educational effort, this type of mass-culture program is extraordinarily effica-

cious. Inexpensive mass-culture methods evolved in this program, together with the use of volunteer help, have made the project practical in economic terms.

815 S. Center (Dr. Phibbs).

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THE CASPER PROJECT—AN ENFORCED MASS-CULTURE STREPTOCOCCIC CONTROL PROGRAM

2. TECHNICAL ASPECTS

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A school culture program has been in full operation in the grade schools of Casper, Wyo., since the fall of 1955 after a pilot study in the spring of the same year. The program was designed to detect children carrying group A streptococci in the nose and throat and to refer them for treatment in the hope that the incidence of rheumatic fever might be reduced. Our results to date indicate that the program has been beneficial, and it will be continued on a permanent basis.

Many studies on the problem of rheumatic fever prophylaxis have been made by other investigators.[1] These studies, in general, have differed from our program in several respects. Previous programs have utilized mass cultures of all children in a classroom or school group at regular intervals without regard to the presence of symptoms[1c]; this approach has been supplemented in some instances by special cultures of ill or absent children. Other programs have been concerned with detection and treatment of streptococcic infections in family groups[1d] or with public education programs.[1e] In the Casper program we have done cultures only for those children presenting specific symptoms or signs on a given day, and have left the decision concerning an individual child to volunteer, specially trained, nonprofessional workers. On occasion we have made cultures for whole classroom

The object of a streptococcic control program is to detect and treat a maximum number of streptococci carriers in the easiest possible way. The child with a positive culture is immediately sent home with a mimeographed form letter to the parents. After treatment is given and the letter initialed by the family physician the child is readmitted to school. It is conceded that a simplified program will not allow identification of all carriers of Streptococcus pyogenes. Nevertheless by reducing the incidence of rheumatic fever appreciably a successful program is established.

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populations or whole family groups in the presence of repeated positive cultures among individual members.

Most previously reported programs have utilized a full-scale laboratory approach to the identification of group A streptococci. The procedures have included the use of enrichment liquid mediums with varying numbers of subcultures and, on occasion, final identification by serologic methods. We have used the simplest approach we could devise and as a result, no doubt, have obtained a higher incidence of both false-negative and false-positive results. Let us emphasize that our immediate objective is reduction in incidence, not eradication, of rheumatic fever. To reach the latter end, logically, we should culture each member of the community every day, and rigidly enforce treatment programs. This being impossible we must compromise by culturing the most productive community group by the simplest technique. We must utilize the least expensive approach, and must use as few highly trained technical persons as possible, since both money and technical personnel are sometimes at a premium. We must educate the public to seek treatment and the family physician to urge it.

It is conceded that a simplified program will not allow identification of all carriers of Streptococcus pyogenes. Some will not be cultured in the first place. Some will receive falsely negative or positive culture reports because of simplified laboratory techniques. Some will be treated inadequately or not at all if the parents or physician are not convinced of the value of the program. Nevertheless if we succeed in reducing the incidence of rheumatic fever by an appreciable amount we have established a successful program.

Materials

We use blood agar plates prepared in disposable 100-mm. plastic Petri dishes with bacto-blood agar base and added human blood in acid-citrate-dextrose solution. We have abandoned use of outdated bank blood and are using fresh blood from "short" donor units or that obtained from therapeutic venesection. There are valid objections to the use of human blood in blood agar plates, but we have been unable to make satisfactory arrangements for a steady supply of defibrinated animal blood. The plates are prepared by laboratory personnel at Natrona County Memorial Hospital. Smaller communities in Wyoming are using commercially available plates of prepared mediums.

Throat swabs are prepared daily by central service personnel of the hospital. Commercial cotton swabs are autoclaved in screw-capped culture tubes. Particular care is taken that the caps are fastened only loosely during autoclaving; as soon as autoclave pressure is reduced the caps are tightened to trap moisture inside the tubes. This is an important step, since complete drying of the swabs and tubes, as would occur under autoclave vacuum, produces large numbers of sterile cultures. We are undertaking a comparative study using swabs prepared in this manner and those prepared in a liquid enrichment medium. Our impression at this time is that use of "dry" swabs, especially if they are thoroughly wetted with mucus from the throat when the culture is taken, produces very nearly the same number of positive cultures as obtained with enrichment mediums. In addition, wet mediums are more expensive and require particular care to avoid contamination of mediums by contact with the handle of the swab stick after the culture is taken.

Mimeographed forms are prepared by hospital personnel. One provides for identification of the school, date, name, grade, and room of child, a simple number coding system to identify the swabs, a column for culture results, and space for listing the reason for culture. The second is a form letter taken by the child to his parents, stating that he is infected by the Streptococcus organism, and advising them to contact the family physician for treatment. Other items such as tongue blades, flashlights, and batteries are also provided. Each day the culture tubes are brought to the hospital laboratory by voluntary workers, who then receive replacement supplies as needed. All stocks are maintained in the laboratory.

Collection of Specimens

Early in the course of our program it was decided that the task of obtaining the cultures and sending them to the laboratory could be assigned to nonprofessional workers. In the first place there were not enough school or public health nurses or physicians immediately available. Secondly, there seemed no better way to enlist the interest and cooperation of the community. The problem was presented before parent-teacher organizations and in the local newspapers, with an extremely gratifying response. A large number of young women, mainly mothers of school-age children, volunteered immediately and have proved invaluable in the program. Interested local physicians were assigned various schools. They have held conferences with the volunteer workers and teachers from each school to explain the program in detail and instruct in the proper procedures for selecting and culturing the children. During the current year a registered, specially trained nurse has been employed on a part-time basis to assist wherever difficulties are encountered in the schools; she also plates the swabs, keeps all records, and performs family follow-ups, relieving the laboratory personnel of these extra duties.

The volunteer women from each school have organized themselves in groups. One or more members appear on a rotation basis at the school each

morning at 9 a. m. The teachers send to the appointed room all students who appear ill or who complain of sore throats or colds. Those children are selected for culture who present one or more of these features even to a very minor degree: fever, swollen tender cervical nodes, postnasal discharge, or inflamed nasopharyngeal mucosa. Cultures are obtained from the involved areas of pharynx or nasopharynx and the capped culture tubes with identification data are taken to the hospital laboratory immediately, where replacement supplies are obtained for the following day. This whole process is usually completed in 30 to 45 minutes.

Laboratory Procedure

The culture tubes for the current day are received by the laboratory technicians. They are arranged in convenient order and plated on blood agar; with practice about 60 swabs per hour can be processed. The contaminated swabs and tubes are returned to the hospital central supply for sterilization, cleaning, and preparation of new tubes.

Each blood agar plate is divided by wax pencil lines into 10 or 12 segments labeled according to a number-letter code to correspond with the swabs. Although the surface area used for each culture is small, this has not proved a serious problem provided the inoculation technique is proper. Care is necessary to avoid too heavy plating; the cotton swab is rolled once at the base of each wedge-shaped area. When an entire plate is so prepared, spreads are made with the finest available wire; only a few strokes of the wire are made from base to apex of each segment. Too many strokes result in too heavy a culture and reading becomes very difficult. There is, theoretically, danger of error from mislabeling or cross-contamination from adjacent areas, but we are not aware that this has been a serious problem. Plating of the swabs begins not more than 30 minutes after the swabs are received in the laboratory and is usually completed by noon. A longer delay might result in unsatisfactory cultures, but we have not found this to be a problem with the procedure described. The occasional culture which does not produce adequate growth is repeated the next day.

The completed plates are incubated until about 9 a. m. the following day, when they are read by one of us (D. L. B.). Identification of streptococcic colonies is made on the basis of gross colony morphology and beta-hemolysis. With experience such colonies are picked rather easily. The organism most frequently confused with Streptococcus on the basis of beta-hemolysis is Micrococcus. Usually micrococcic colonies are much larger, produce a relatively narrower band of hemolysis, and present a characteristic rounded, white, opaque appearance. Streptococcic colonies are small, semitranslucent, and develop wide, sharply demarcated zones of hemolysis. Some strains of micrococci produce very small colonies which are difficult to identify; formerly we preferred to call these positive if doubt existed, on the theory that it was better to overdiagnose than underdiagnose. During the current year, when subcultures have been made on all suspect colonies, this has been a lesser problem since the gross differentiation is much easier on the multiple colonies of a pure culture. The number of streptococcic colonies will vary from one or two per segment to an essentially pure culture. A culture with even one clear-cut colony of streptococci is read as positive.

During the first year of the program, all cultures containing beta-hemolytic streptococci were reported positive. This was known to be somewhat inaccurate since gross differentiation between streptococci of Lancefield's group A and beta-hemolytic strains of Lancefield's groups B, C, D, and G is not possible, and only the group A strains are of significance in this context. In most cases the problem is primarily one of differentiation of group A from group D strains; numerically groups B, C, and G are not commonly found under these circumstances. At intervals during the first year, a series of subcultures of streptococcic colonies to blood agar and eosin-methylene-blue agar was performed; with this procedure group D colonies will ordinarily grow on eosin-methylene-blue agar while group A strains will not. About 18% of our streptococci strains were of group D. With this approach a certain number of children who were treated (with penicillin as are all children in this series) proved to harbor beta-hemolytic strains on routine reculture performed after 10 days.

These strains, isolated on reculture, were uniformly subjected to differential subculture, and uniformly proved to belong to group D. The problem became worse as time went on and as the relative number of group A strains isolated was reduced by continuing treatment of carriers. It did not seem easily soluble, since the technique was cumbersome and time consuming. In the fall of 1956 we became aware of an identification procedure based on the fact that most group A strains are inhibited when grown on blood agar plates implanted with bacitracin disks of low (2 unit) concentration while most strains of the other groups are not.[2] This procedure is subject to some error, particularly in identification of groups B, C, and G; the most common error, however, tends to falsely identify a given strain as group A, so that the method seems ideally suited for our program.

Since the fall of 1956 colonies of all presumptively positive cultures are transferred directly to quadrants of a blood agar plate on the morning they are read; bacitracin disks are implanted and

final readings provided the following morning. In this way only a single subculture transfer need be made and the procedure is quite satisfactory. Initially the results of this technique were compared with those of the double-subculture technique with excellent agreement. The delay between culture and report is increased to 48 hours, and to 72 hours over a week-end, but this appears unavoidable.

The identification subcultures were undertaken with some doubts, since the procedure is time-consuming when 40 or 50 positive cultures are encountered in a day. As the program proceeded during 1955 and 1956, the number of positive cultures was gradually reduced to an average of 8 to 10 per day; the subcultures can be prepared under these circumstances in about 25 minutes.

Initially individual colonies were transferred to enrichment broth, and then to the agar plates for identification. This only consumed more time and materials and did not appear beneficial. With practice and a small loop, even a single colony close to its fellows may be satisfactorily transplanted. Occasionally transplanted colonies fail to produce growth; these are read as group A, again on the theory that it is better to overdiagnose than to underdiagnose. Since we have begun to differentiate group A from other strains we have encountered only one child who, having received adequate penicillin treatment, had a persistently positive culture. The tonsils were much enlarged in this child; he underwent tonsillectomy and no more positive cultures have been obtained.

Reporting

Each morning the laboratory secretary reports by telephone the names of children with positive cultures to the principal's office of the proper school. The child is immediately sent home with a mimeographed form letter to the parents. After treatment is given and the letter initialed by the family physician the child is readmitted to school; since most children are symptomatic at least one day of school is usually missed before the parents allow return. Each child with a positive culture routinely receives a reculture 10 days after the first.

With some frequency cultures from the same child will prove positive repeatedly over a period of weeks or months. In such cases arrangements are made by the program nurse through the family physician to make cultures for all members of the family involved. This is done either by appointment in the hospital laboratory or, if convenience dictates, by the workers at one of the schools. As a matter of interest, persons who handle the cultures are urged to have cultures made themselves at rather frequent intervals. Our laboratory personnel and the program nurse frequently had positive cultures in the early stages of the program and have developed a healthy respect for precise bacteriological technique.

Economic Aspects

It is estimated that, considering only the actual cost of materials used, the throat cultures can be made for between 8 and 10 cents per culture. This does not include any estimate for the time donated by the volunteer workers, the pathologist, or the members of the county medical society rheumatic fever committee who donate their time but does include the cost of labor by hospital employees who prepare materials; the program nurse is paid separately. No strict accounting of costs is kept routinely; the nurse is paid from available funds and the hospital general fund receives a lump sum at the end of the school year to help defray its expenses. The first year $500 was available from the Wyoming Heart Association. During the current year $1,000 was received, in addition to which $500 was received from the local United Fund organization and $500 from Wyeth Laboratories.

The estimated total cost during the first year (roughly 8,000 cultures) was approximately $720, about a $220 loss to the hospital. This was considered a legitimate part of the hospital's community service. Local business concerns that have been asked for help in preparing educational material for this program have uniformly refused payment for their services. By far the majority of children with positive cultures are treated by their family physicians at the usual fee, and no attempt will be made to establish a "free treatment" program. The charity cases receive treatment without charge or at reduced charge from their family physicians, as usual. Free penicillin is available from the Wyoming Department of Health for use in such cases.

Summary

A program for culturing the throats of grade school children to detect beta-hemolytic streptococci has been in successful operation in Casper, Wyo., since 1955. The program has been established so that there is minimum expenditure of money, materials, and technical help; simplified procedures have been employed wherever possible. The object has been to detect and treat a maximum number of streptococci carriers in the easiest possible way.

Results of our studies indicate that the incidence of streptococcic infections and of acute rheumatic fever is lower in this community since the program was started. In addition there has been widespread and desirable local dissemination of information to the public about these diseases. The program will be continued indefinitely.

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BRUCELLOSIS AND HEART DISEASE

IV. ETIOLOGY OF CALCIFIC AORTIC STENOSIS

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Because of inconsistencies in the popular theories regarding calcific aortic stenosis, another explanation has been sought for this common form of valvular heart disease. The valve lesions encountered after fatal brucellosis closely resemble those in calcific aortic stenosis. A similar type of chronic aortic valve disease was recognized in nine patients who recovered from brucellosis. Calcific aortic stenosis is chiefly a disease of males, corresponding to the sex incidence of brucellosis. For these and other reasons it is proposed that calcific aortic stenosis is, in most cases, a sequel of brucellosis.

Calcareous disease of the aortic valve is characterized pathologically by nodularity, calcification, and deformity of the cusps and commissures and by irregular distortion of the valve orifice. Because of the fusion and rigidity at the commissures, aortic stenosis is the usual effect (fig. 1). In those cases in which destruction of a commissure causes sagging of a cusp so that the orifice cannot close perfectly, there will be aortic insufficiency as well as stenosis (fig. 2). Left ventricular hypertrophy is often extreme. Although physical findings are sometimes minimal, such symptoms of serious heart disease as angina and syncope are usually evident. Sudden death is common in this group, often a result of complete heart block.

The reported frequency of calcific disease of the aortic valve varies in different autopsy series, depending upon several factors, chiefly the age of the group on which autopsy is done. As to its relative frequency, Clawson, Noble, and Lufkin [1] noted that calcified nodular aortic valve deformity (without involvement of other valves) comprised 41% of all healed valve deformities seen on the autopsy service at the University of Minnesota. At the George Washington University Hospital these cases, without involvement of other valves, comprise 26% of all healed valve deformities, as compared with 29% pure mitral stenosis and 45% combined valve lesions.

Calcium deposition in nonosseous tissue is ordinarily a result of a series of local chemical or physical changes. These changes may begin with either lipoid deposits (as in atherosclerosis of the aorta), necrotic tissue (as in tuberculous nodes), or fibrin (as in old thrombi). Thus, theoretically, calcareous disease of the aortic valve may be a result of a degenerative process comparable to atherosclerosis of the aorta or of an inflammatory process such as rheumatic valvulitis or bacterial endocarditis.

About 20 to 30% of patients with calcific aortic stenosis give a history of prior joint disease. For this reason, and because of the presence of certain gross and microscopic "rheumatic stigmata" in the heart, rheumatic fever has been considered by many to be the cause of the residual valve deformity. Since identical clinical and pathological manifestations may be produced by other diseases, however, it is obviously impossible to distinguish the residual lesions of rheumatic fever from those due to certain other illnesses. This point has been elaborated in the first paper in this series.[2]

Calcium deposits in relation to vascular endothelium naturally suggest a relationship to atherosclerosis. However, the precursor phase consisting

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of lipoid deposits is not known to occur, and the valvular changes are ordinarily not associated with extensive atherosclerosis of the aorta.

The appearance of the valve lesions suggests that they are a result of bacterial endocarditis: atherosclerosis and rheumatic fever are ordinarily not so destructive. On the other hand, bacterial endocarditis is generally believed to be a fatal disease unless its course is modified by antibiotic therapy. A natural tendency to heal and calcify is incompatible with current concepts of bacterial endocarditis.

In 1941, I performed an autopsy on a 51-year-old male who had had an intermittent febrile illness for 18 months before his death (case 2 in the series of probable cases of fatal brucellosis not proved by culture, reported by myself and Belter [1]). At one time during his illness this patient's serum agglutinated Brucella antigen at a titer of 1:10,240. Terminally there were the murmurs of aortic valve disease, and death was a result of congestive heart failure. Postmortem examination revealed an essentially chronic form of endocarditis limited to the aortic valve. There were old infarcts in the kidneys and spleen. This case raised the question whether brucellosis, a disease often marked by recurring bacteremia for many months, might be a cause of calcific aortic stenosis. To check this possibility, a series of investigations have been made.

Fig. 1.—Calcareous disease of aortic valve producing extreme stenosis of orifice (viewed from above, unopened).

Autopsy Findings in Fatal Brucellosis

In a review of the world literature on fatal brucellosis [2] 42 culturally proved fatal cases of brucellosis were found in which there were adequate autopsy data. These cases are summarized in table 1. It should be noted especially that, among the 18 cases of fatal Brucella abortus infection, endocarditis was present in 17, and in 16 instances the aortic valve was involved (fig. 3). In 12 of these cases the author specifically noted that calcium was present in the affected valve cusps or vegetations.

In some cases there were microabscesses within the nodular hyaline valve cusps. In other cases necrosis was minimal and there were focal hyaline areas and coalescent masses of calcium (fig. 3) closely resembling the changes in the inactive valve lesions of calcific aortic stenosis. The necrotic, hyaline, and calcific lesions in the aortic valve in brucellar endocarditis closely resemble the lesions which have been described in the spleen,[4] lungs,[5] and kidneys [6] in brucellosis and from which Brucella have been cultured.

Table 1.—*Autopsy Findings in Fatal Brucellosis*

	Total Cases	Cases of Endocarditis	Aortic Valve Involved
Culturally proved, due to			
Br. abortus	18	17	16
Br. melitensis	13	9	5
Br. suis	7	3	2
Undetermined strain	4	4	4
Not culturally proved*	15	10	7

* In each case, serum agglutinated Brucella antigen in dilution of 1:500 or higher.

From examination of these cases one can conclude that bacterial endocarditis is the chief cause of death in fatal brucellosis; the aortic valve is primarily affected; the affected valves usually contain calcium deposits.

Aortic Valve Lesions Following Nonfatal Brucellosis

Through the cooperation of numerous clinical colleagues, and also from a study of causes of death in veterinarians,[7] 10 cases have been found in which chronic valvular heart disease followed by some years an illness diagnosed on clinical grounds as brucellosis. These cases will be reported separately.[8] Nine of these patients had a pure aortic lesion and one of them a pure mitral lesion. The average age at the onset of brucellosis was 40.7 years. The average age at the diagnosis of heart disease was 51.5 years, at death (six cases) 59.5 years, and of the four survivors at the time of study 54.7 years.

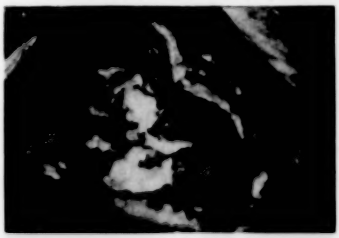

Fig. 2.—Calcareous disease of aortic valve resulting in deformity of commissures and aortic insufficiency (viewed from above, unopened).

In four cases the clinical diagnosis of chronic valvular disease was confirmed by postmortem examination. The valvular lesion in three of these patients

was in no way distinguishable from that of the usual calcareous disease of the aortic valve (fig. 4); the fourth patient had mitral stenosis.

Hence we can conclude that brucellar endocarditis is essentially a chronic disease. The active bacterial phase may heal leaving a residual valve lesion.

Immunological Studies in Patients with Calcific Aortic Stenosis

A controlled study was undertaken to determine whether there was immunological evidence of prior brucellosis in patients presenting calcific aortic stenosis.[9] Twenty-four patients with aortic stenosis were investigated. Most patients were from the outpatient department of the George Washington University Hospital; a few were from the surgical service at Georgetown University Hospital. Blood samples for Brucella agglutination were taken from each patient and intradermal tests with brucellergen were done. Twenty-three other outpatients were selected as controls; they had no evidence of valvular heart disease and were matched with the test patients as to sex and as nearly as possible as to age.

While the results (table 2) are by no means convincing, it appears that there were probably 2 patients with definite brucellosis among the 24 with aortic stenosis. (Carpenter[10] has shown that patients with unspecified cardiac diseases have a higher rate of skin sensitization to Brucella antigen than do patients with other diseases.) Although the evidence is not conclusive, we can say that immunological studies on patients with calcific aortic stenosis reveal evidence of brucellosis in some instances.

TABLE 2.—*Immunological Studies in Calcific Aortic Stenosis*

	Patients with Aortic Stenosis	Control Patients
Brucella agglutination		
Negative	20	21
1:20	1	2
1:40	1	0
1:640	2	0
Brucellergen skin test		
Negative	22	20
Positive	2	3

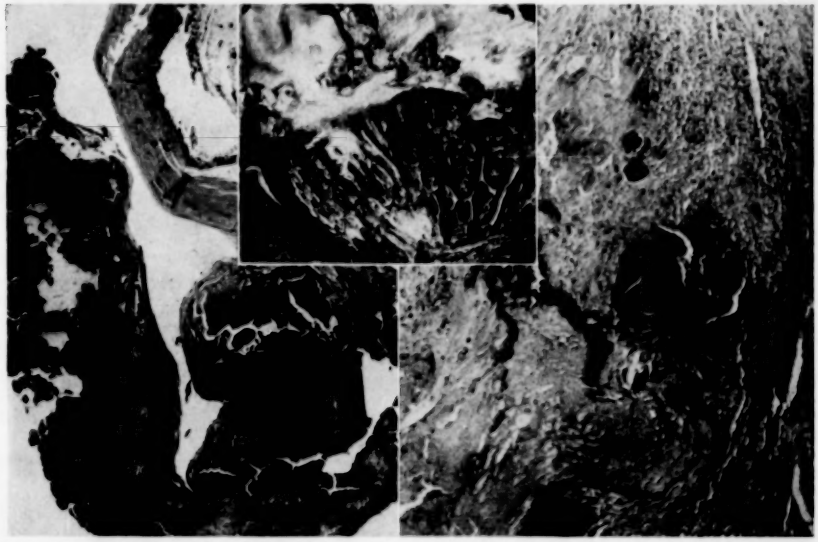

Fig. 3.—*Insert*, chronic endocarditis due to Brucella abortus. Aortic valve is chiefly affected. *Left*, section through aortic valve lesion showing extensive calcific deposits. *Right*, higher magnification of aortic valve lesion in fatal brucellosis, showing necrosis and inflammatory reaction adjacent to areas of hyalinization and calcification.

Sex Incidence of Calcific Aortic Stenosis and Brucellosis

From the evidence presented it seems reasonable to conclude that calcific aortic stenosis may, in some cases, be a residual lesion of brucellar endocarditis.

In order to determine the relative importance of the several possible causative agents, I have compared the sex incidence of each of the suggested causes with the over-all sex incidence of calcific aortic stenosis. A summary of this comparison reveals some relevant data. Of 822 patients with calcific aortic stenosis, 73% were male [11]; of 3,129 patients with rheumatic fever and rheumatic heart disease, 50% were male [12]; of 408 patients with subacute bacterial endocarditis, 49.5% were male [13]; and of 2,409 patients with brucellosis, 79% were male.[14]

Rheumatic fever makes no distinction between the sexes,[12] nor does it show a tendency to involve a particular valve in a certain sex (Cohn and Lingg [15]). There is no significant difference in the incidence of subacute bacterial endocarditis in the two sexes.[13] Brucellosis has a remarkable predilection for the male. This is due presumably to the occupational nature of the infection in most cases, as noted by Hardy and co-workers,[16] Jordan,[14] and others. (Reliable figures for the sex incidence of atherosclerosis are not available because of the subjective nature of the observations. Males seem predominantly affected in early adulthood, but in later years, at the age when calcific aortic stenosis appears, the sexes are generally believed to be involved about equally.) Hence, the sex incidence of calcific aortic stenosis is unusual, and corresponds closely with that of brucellosis.

Other Studies

A search for evidence of heart disease in animals infected with Brucella has been unsuccessful. Apparently no such studies have been done previously. Examination of the hearts from 100 cattle slaughtered because they had a positive reaction for Bang's disease showed no evidence of cardiac lesions.[7] Since these animals were killed for economic reasons rather than because of illness, it is perhaps not significant that no lesions were found. Other species may yield more significant results.

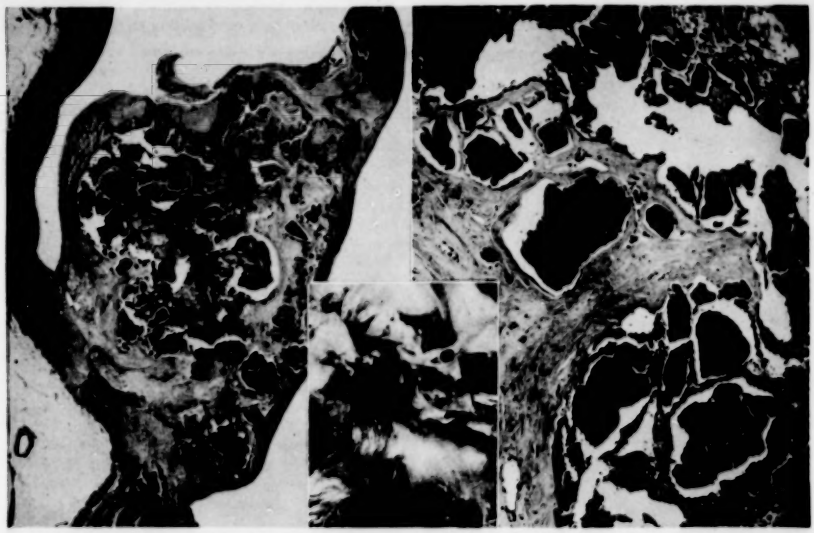

Fig. 4.—*Insert*, calcific aortic stenosis at age 76, many years after prolonged febrile illness diagnosed as brucellosis. *Left*, section showing nodular calcific deposits in aortic valve cusp. *Right*, higher magnification of residual aortic valve lesion after nonfatal brucellosis. Inflammatory reaction has disappeared leaving scar tissue, calcium deposits, and dilated vascular channels.

Although it seemed unlikely that bacteria could be demonstrated in the hyaline and calcified valve cusps of calcific aortic stenosis, we [17] considered it worth a try. In six cases one or more of the cusps were removed post mortem, with aseptic precautions taken. The calcified masses were ground with mortar and pestle, and a suspension of this material was then prepared. Portions were inoculated upon plain trypticase soy agar and upon trypticase soy

agar to which crystal violet (1:700,000) was added for inhibition of contaminants. Other portions of the suspension were injected into guinea pigs. Blood samples were withdrawn from the pigs at four weeks and at six weeks and were tested for Brucella agglutinins with use of the antigen supplied by the Bureau of Animal Industry. The animals were killed at six weeks and their organs were examined grossly. Material was taken from the spleen, regional lymph nodes, liver, and testes and inoculated on trypticase soy agar as before. All plates were incubated under 10% carbon dioxide tension and were held for 10 days before discarding. All studies were negative.

It is uncertain how frequently valvular heart disease develops during the course of nonfatal brucellosis. It is probably more common in the severe recurring infections based on occupational exposure than in the milder infections due to casual contact with milk products. Evans and I [18] have studied several patients with mild brucellosis and found no sign of valvular heart disease. To determine the frequency of this sequel, a large series of patients with brucellosis should be followed over a long period of time. Such a study can best be carried out in an area where the disease is endemic. Detailed examinations of the heart would be necessary to detect the residual valve lesion, since physical signs may be minimal, misleading, or even completely absent in calcific aortic stenosis.

Summary and Conclusions

There is evidence to the effect that calcific aortic stenosis often is the residual lesion of brucellar endocarditis, chiefly due to the Brucella abortus strain. This evidence is as follows:

In a number of cases, calcific aortic stenosis has followed a febrile illness diagnosed as brucellosis. In fatal brucellosis, chronic endocarditis is an almost constant finding. The aortic valve is primarily affected and there is a natural tendency for the ulcerated valves to heal and calcify. The gross and microscopic appearance of the aortic valve in brucellar endocarditis is almost identical with that in calcific aortic stenosis. The granulomatous lesions in other organs during brucellosis, from which Brucella have been cultivated, closely resemble the valve lesions in calcific aortic stenosis. Some patients with calcific aortic stenosis show a high titer of agglutinins against Brucella in their serum. The sex incidence of calcific aortic stenosis is unusual and corresponds with that of brucellosis rather than rheumatic fever.

Brucellosis is thus suggested as the chief cause of calcific aortic stenosis on the basis of pathological, clinical, and immunological studies. These observations open up new vistas for the prevention of heart disease.

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COMPENSATION FACTOR IN LOW BACK INJURIES

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and
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The histories of 509 patients treated for low back injuries were studied for differences that might be related to compensation. Only 55.8% of the 272 patients receiving compensation were rated as improved at time of discharge, as compared to 88.5% of the 237 patients not receiving compensation. Over two-thirds of the patients who did not receive compensation had appeared for treatment during the first month of symptoms, whereas only about one-half of the patients who received compensation had been seen at this point. The mean number of treatments received by the compensation group, both men and women, greatly exceeded that for the noncompensation group. Some patients in the compensation group responded well to conservative management and returned to their jobs after a minimum number of treatments, but in others there appeared to be a difficulty within the basic personality structure. Psychiatric experience with the latter type has not been encouraging. Throughout the study, the women expecting compensation showed the worst response to treatment while receiving the greatest number of treatments. Prompt adequate diagnosis and early adequate conservative treatment are recommended as essential in handling these patients, but there is real need for further investigation of the medical, psychological, and legal aspects of this complaint.

It has long been the impression of physicians who treat back injuries that patients receiving compensation are often more difficult to cure than those who are not eligible for such benefits. We felt that it might be of interest to see if this clinical impression could be substantiated by studying similar groups of patients with and without compensation who received the same treatment and to determine what factors might be involved.

Over 500 patients treated in the physical medicine department of Baylor University Hospital during a five-year period were used for the study. Of the 509 patients, it was found that 54% were eligible for compensation and 46% were not, which represented a sufficiently equal distribution for our study. As might be expected, there were many more men than women in the compensation group. Patients not receiving compensation were about evenly distributed with regard to sex (table 1).

TABLE 1.—*Number and Percentage of Patients Receiving and Not Receiving Compensation for Injury*

	Sex	Patients No.	Patients %
Receiving compensation	M	213	42.0
	F	59	12.0
Not receiving compensation	M	116	22.8
	F	121	23.2
Total		509	100.0

The majority of the patients were referred for physical therapy by other physicians, mostly orthopedic surgeons or neurosurgeons, who had initially established the diagnosis of low back pathosis due to injury. Many of the patients had already received some treatment, such as bed rest at home, some form of heat, or back manipulation, prior to referral.

Only those patients were included in this study who received a minimum of at least five treatments, for three reasons: 1. Patients who became symptom-free with fewer than five treatments might well have improved without treatment. 2. The group receiving fewer than five treatments included many patients who had severe lesions requiring surgery and were therefore not suitable candidates for conservative management. 3. Patients who came to the physical therapy unit less the five times provided small opportunity for follow-up.

From the Department of Physical Medicine and Rehabilitation, Baylor University Hospital.

Read before the Section on Physical Medicine at the 106th Annual Meeting of the American Medical Association, New York, June 6, 1957.

Symptoms

Only patients with an acute back injury, that is, those who could relate the onset of symptoms to a particular incident, were included in this study. The most common symptom was pain in the lower back, often with radiation into one leg and sometimes into both legs. Many patients complained of back pain after coughing or sneezing. Almost all patients demonstrated some degree of limitation of straight leg raising. The majority did not exhibit any significant diminution of deep tendon reflexes. Many patients noted numbness to pin prick over

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portions of the lower extremities, though this usually did not conform to dermatome distribution. Few patients had true weakness of the dorsiflexors of the foot. Nearly all had limitation of back motion, ranging from that noted only on testing to constant assumption of the flexed position. No effort was made to exclude patients with a clinical diagnosis of possible ruptured intervertebral disk, although the most common diagnosis was muscular or ligamentous sprain.

Treatment and Hospitalization

Although one might expect that more patients with compensation would receive hospitalization than those without, this was found not to be true in this series. In the compensation group 73% were hospitalized, and in the noncompensation group 76% were hospitalized. If hospitalization can be taken as an index of the severity of symptoms and thus of the severity of the injury, there existed essentially no difference between patients receiving compensation and those not receiving compensation in this regard.

The majority of the hospitalized patients were at bed rest in the jackknife position, some with leg traction, and many received muscle relaxants. In the Physical Medicine Department, treatment for the patient with low back injury was started with 30 minutes of heat, usually short wave diathermy unless contraindicated. An effort was made to position these patients comfortably either in a side-lying position with the knees flexed or in the prone position with ample support under the abdomen in the form of pillows so that the back was semiflexed. The heat treatment was followed by massage of the deep sedative type, as tolerated by the patient. Some patients also received electrical stimulation to the involved back muscles.

As soon as the patient had passed the most acute stage, low back flexion exercises were added. It was usually most satisfactory to start these exercises with the patient lying supine with hips and knees flexed in order to eliminate the extensor action of the iliopsoas muscle on the lumbar spine. In order to flex or flatten the lumbar spine, the following exercises were used: 1. The simplest exercise was contraction of the gluteus maximus muscles, also called "pelvic tilt." 2. The next exercise consisted of flexion of the neck and upper trunk through a limited range, resulting in strengthening of the abdominal muscles, and also flexion of the lower spine. The range was carefully limited in order to avoid contraction of the iliopsoas and resulting extension of the lumbar spine. 3. The last exercise consisted of passive hip and knee flexion. This was done from the same position by having the patient grasp his knee with both hands and pull it toward his chest, first one leg at a time and finally both simultaneously. All exercises were carefully graduated and were performed "to the point of pain" only.

As the patients' conditions improved, they were also taught the basic principles of proper body mechanics to enable them to avoid extension of the low back in all forms of activities, such as sitting, walking, and lifting. Exercises involving hamstring stretching, such as touching the toes with knees extended either sitting or standing, were generally avoided.

Results of Study

The patients in each group were analyzed with regard to the following factors: improvement following treatment, duration of complaint before treatment was started, relationship of the duration of symptoms before treatment to the results of treatment, number of treatments received, and results of treatment at late follow-up.

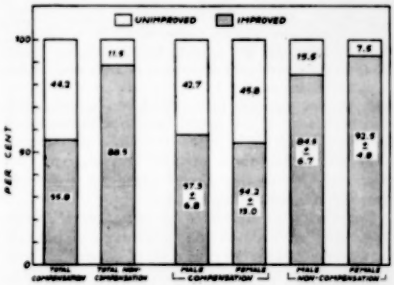

Fig. 1.—Results of treatment in patients who received compensation and in those who did not.

Results of Treatment.—The results of treatment were classified as either improvement or no improvement largely on subjective grounds, since objective improvement is of little value if the patient is having too much pain to return to work. Thus, a patient was considered unimproved if he or she continued to complain and failed to resume normal activities, including work, regardless of objective improvement. This method has previously been used in many studies of the management of low back pain.[1]

Figure 1 shows a comparison of improvement for patients who received compensation and for those who did not as a whole and also for each group divided according to sex. Only 55.8% of the patients receiving compensation were rated as improved at discharge, as compared to 88.5% of the patients not receiving compensation. The observed difference in improvement between men who anticipated compensation and those who did not was 27.2%, while the difference to be expected on the

basis of chance was only 9.6%. For the women, the observed difference was 38.3%, while the expected difference was only 13.8%.

Duration of Complaint Before Treatment.—Figure 2 shows that over two-thirds of the patients who did not receive compensation, both male and female, had appeared for treatment during the first month of symptoms, whereas only about one-

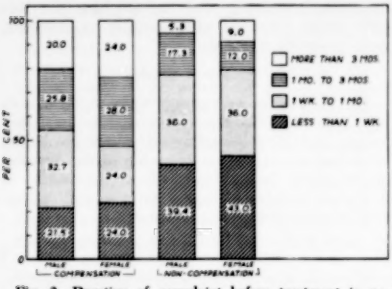

Fig. 2.—Duration of complaint before treatment in patients who received compensation and in those who did not.

half of the patients who received compensation had been seen at this point. Less than one-tenth of the first group were referred to the department after more than three months of symptoms, but over one-fifth of the second came for treatment over three months after injury.

Correlation of Results with Duration of Symptoms.—Figure 3 shows the percentage of patients improved for different durations of complaint, both for those who received compensation and for those who did not. Both groups showed a definite decrease in improvement among the patients appearing for treatment after more than one month of symptoms. This drop was especially marked in the compensation group.

The fact should be noted, however, that even the patients who received compensation who were seen for physical therapy during the first week after injury did only slightly better than those who did not receive compensation who were seen three or more months after their injury. Thus, though the patients, in general, responded better to treatment when it was initiated early, this factor was not the only key to the recalcitrant symptoms of the patient who received compensation.

Number of Treatments.—The number of treatments the patients received varied from the accepted minimum of 5 to 91. The mean number of treatments was calculated for each of the four groups. There was a striking similarity between the mean number for men (18) and women (18.3) in the compensation group and those for men (9.8) and women (11.1) in the noncompensation group. As can be seen, both men and women in the compensation group received a significantly greater number of treatments than did their counterparts in the noncompensation group (observed difference among men, 8, and among women, 7). Over one-half of the patients receiving compensation were dismissed from physical therapy after 13 treatments; over one-half of the patients not receiving compensation were dismissed after 9 treatments.

An attempt was made to correlate the number of treatments with improvement, but unfortunately no definite relationship could be established. The mean number of treatments for patients who showed improvement essentially did not differ from that for those who did not in the same group or from that of the group as a whole.

The mean number of treatments was also correlated with the duration of symptoms before treatment was started. Figure 4 shows a definite relationship in the compensation group; those who waited the longest before treatment received the greatest number of treatments. The correlation for the noncompensation group was not so significant because of the small number of patients in this group who had symptoms for more than three months before treatment was started.

Late Follow-up.—A late follow-up on the results of this study was obtained from the records of the referring physicians, either on discharge of the patient or on the last office visit. This included 358 of

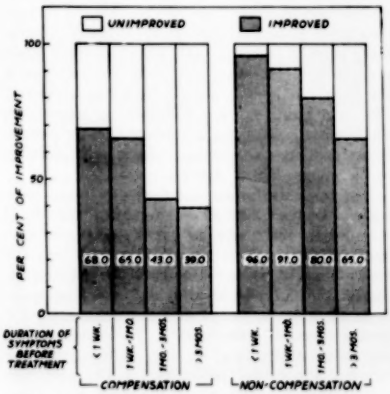

Fig. 3.—Correlation of results of treatment with duration of symptoms in patients who received compensation and in those who did not.

the 509 patients in this series, and these results are shown in table 2. The time lapsed after dismissal from physical therapy varied from a few weeks to several years. When the patients who had had surgery were excluded from the evaluation, the percentage of patients showing long-term improve-

ment was similar to that shown originally. Figure 5 shows that the follow-up results tended to get slightly better for the patients not receiving compensation, while those for the patients receiving compensation tended to become somewhat worse.

Comment

The results obtained in this study of 88.5% improvement among patients not receiving compensation are similar to those of Coyer and Curwen,[12] who reported 88% of their patients as improved; Breck and Palafox [17] reported 87% of patients improved, and Haggart and Grannis [14] reported 91% improved. However, the improvement of 55.8% found among our patients who received compensation is far different from that of 87% reported by Jessup and co-workers.[15] In this regard, it must be emphasized that the patients of these other observers were all ambulatory and were treated at work, while three-fourths of the patients in this study were hospitalized. This reflects a probable difference in extent of injury. Our study may have excluded many of the patients with minor injuries by the imposed minimum of five treatments.

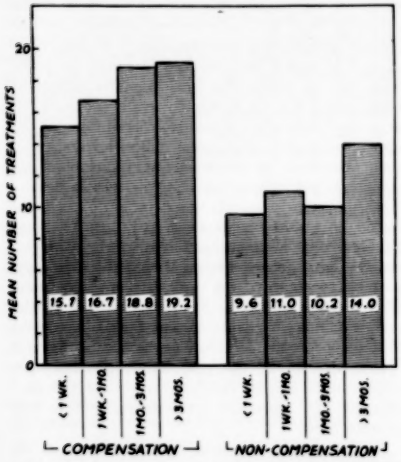

Fig. 4.—Correlation of duration of symptoms with number of treatments in patients who received compensation and in those who did not.

Results show that the longer a patient waits before treatment the smaller is the probability of his improving, regardless of whether he expects compensation or not, and that generally the patients who receive compensation are referred for treatment later than those who do not. The reasons for this are hard to explain; certainly they are not financial, and the delay may cause many undesirable consequences. Admittedly, the more severely injured patients are eventually hospitalized for an intensive treatment program, but one gets the impression that many of these patients receive inade-

TABLE 2.—*Percentage of Patients Available for Late Follow-up Study, with Results*

	Receiving Compensation		Not Receiving Compensation	
	M	F	M	F
Total, %	53.0	66.0	64.0	61.0
Patients with surgery, % of total	21.6	11.1	14.2	12.1
Patients improved at late follow-up, %	44.2		91.1	
Patients improved at immediate follow-up, %	55.8		88.5	

quate therapy for a prolonged period of time. Even when an attempt is made to give physical therapy, this frequently consists of the application of heat from a heat lamp or diathermy machine alone. This is certainly not adequate, but the patient considers it to be "physical therapy," and, when he is finally referred for more intensive treatment, he has developed a prejudice against physical therapy which must be overcome. From this standpoint, it would often be preferable if these patients received no treatment rather than inadequate therapy, and certainly the latter should not be continued over prolonged periods of time. Otherwise, many patients become extremely resentful toward their employers, their doctors, or both and lose their motivation to return to work. If a doctor is treating a patient without being able to provide an intensive

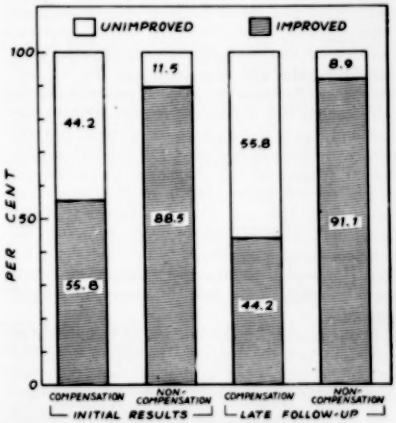

Fig. 5.—Comparison of results of treatment at immediate follow-up and at late follow-up in patients who received compensation and in those who did not.

treatment program, there appears to be a danger point at about one month, after which results of treatment fall off sharply for patients in the compensation group.

Although results are worse for patients who are referred for treatment after three months or more, it is usually still advisable to give them a trial of adequate treatment, since it has been shown that over one-third of them can be improved sufficiently to return to work. Of course, if the same treatment could be provided within the first week after injury, almost twice as many would recover. Providing the patient with early treatment is especially important if he is receiving compensation. Another factor in successful treatment is an early, adequate preparation by the physician. The earlier an accurate diagnosis as to the need for possible surgery can be obtained the easier it becomes to treat the patient. It is not an uncommon experience for a patient to get well after myelography failed to demonstrate any obvious defect. This should not be interpreted as a recommendation for routine myelography, since many patients become disabled by the mere insertion of a needle into the spine. However, in questionable cases, better results would undoubtedly be obtained more quickly if this procedure were done. In this respect, electromyography may prove helpful when it becomes more generally available. Shea and co-workers [2] have shown the possibility of demonstrating intervertebral disks with this technique. In our own experience, electromyography has proved a definite advantage in that it does not require lumbar puncture and insertion of radiopaque material and thus eliminates some of the physiological and psychological trauma of the diagnostic procedure. Of course, even a person with a small protruded intervertebral disk can often be treated conservatively, and, as Barr [3] pointed out, the results are not necessarily proportional to the size of the defect. However, if conservative management fails to provide relief, it is best to resort to surgery promptly.

In the analysis of the number of treatments received by patients, we were unable to determine an optimal number of treatments, since there was no correlation possible between results of treatment and the number of treatments given. Although there may be no ideal treatment time, we feel from our clinical impressions that a series of 18 treatments or a period of three weeks of intensive care, including bed rest and adequate physical therapy, constitutes a fair trial of conservative management. Of course, if the patient is improving under this program, treatment should definitely be continued. But a patient who does not get any relief from these measures during that period should be viewed with considerable concern. He probably requires surgery, or perhaps his psychological problems are so fixed that little help can be expected from further treatment.

Apparently, as a group, the patients suffering acute back strain who receive compensation present different psychological problems from those who do not receive compensation yet whose injuries may be the same. Yet some patients in the former group respond well to conservative management and return to their jobs after a minimum number of treatments. The difficulty appears to lie within the basic personality structure of the individual receiving the injury. For some patients, a back injury seems to present a way of "getting back" at the employer. Once a cash settlement is made, the back pain and disability often subside rapidly. However, with rare exceptions, these patients are not malingering; rather, they seem to be suffering from a compensation neurosis. In the patient who receives compensation it is always important to watch for evidence of emotional problems. In our series, the most common symptoms noted were the neck tension syndrome with its associated headache, dizziness, paresthesias of the upper extremities, and visual difficulties and, also, such symptoms as blackouts, gastrointestinal upsets, bizarre paralyses, and extreme nervousness.

The question arises whether psychiatric treatment would be of help in overcoming the problems of patients with a compensation neurosis. Unfortunately, the usual experience is that these patients go to a psychiatrist only with extreme reluctance. Even if the patient can be persuaded to go, the main function of the psychiatrist is usually to confirm the presence of either an anxiety state or a hysterical reaction. The patients are generally not good candidates for psychotherapy, and the psychiatrists are generally understandably reluctant to treat them.

In this regard, physical therapy often can do more than directly affect the injury to the muscles and ligaments of the back. Adequate physical therapy may prdvide an "out" for the patient's psychological problems if it is started early enough and carried out properly. In our experience, it is well to encourage this effect by the general approach to the patient. Such an approach consists of maintaining from the outset the attitude that the back disability is only temporary and of recommending early settlement of the case, as also was suggested by Fetterman [4] and Jones.[5] It appears that one can safely recommend early financial settlement to the patient with provision for surgery if it be needed, since the passage of time does not greatly change the results of formal physical therapy in the majority of patients.

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It might be advisable to stress that "early" settlement refers to prompt settlement after diagnosis and a fair trial of adequate treatment and not to settlement immediately after the injury. If an insurance company attempts settlement immediately, the patient often develops a far greater psychological problem, since he has the feeling that the company is trying to "put something over" on him and is not giving him a fair chance of recovery.

It was interesting to note that, throughout this study, the women expecting compensation for their injuries have shown the worst response to treatment, while receiving the greatest number of treatments. Apparently, many of them resent the fact that they are required to hold a job, and there seems to be no motive for the women with compensable back injuries to return to work. On the other hand, the women with noncompensable back injuries show more improvement than the men, perhaps because there might be less undesirable pressure on them after recovery. In discussing the work of Haggart and Grannis, Aitken [14] noted this same unfortunate trend in the women who were industrial workers and who underwent intervertebral disk surgery. Among 36 women, only 4 ever returned to work. These patients are truly discouraging to work with, both as a group and as individuals.

The compensable back injury is so common and its economic implications are so far-reaching that there is a real need for further investigation. For the present, the following suggestions may be of value in handling these patients: The employer should make every effort to provide prompt accurate diagnosis and early adequate conservative treatment. The insurance company should maintain a cooperative attitude toward the patient's treatment program. Litigation should be avoided if at all possible, since the engaging of a lawyer often seriously retards the patient's recovery. The physician should encourage an early settlement.

Summary

Among 309 patients with acute low back strain treated by conservative means, 54% were eligible for compensation and 46% were not. Patients who received compensation were referred for treatment longer after their injury than were patients who did not receive compensation. Eighty-eight per cent of the latter group improved with treatment, as compared to only 55.8% of the former, and patients with compensation received a significantly greater number of treatments than did those without, although hospitalization was similar for both groups. There was a correlation between the duration of symptoms before treatment and lack of improvement, and results of treatment at late follow-up were very nearly the same as those at discharge from physical therapy.

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TREATMENT OF PULMONARY TUBERCULOSIS.—In the long-term therapy of pulmonary tuberculosis, isoniazid, without any companion drug and despite declining susceptibility in successive sputum cultures, is about as effective as the old streptomycin-PAS combination. It is, to be sure, not demonstrably superior, and if isoniazid could be used only in this way, it might be considered to have added little except for its lower toxicity and its much greater practicability. When isoniazid is administered concurrently with either streptomycin or PAS, however, the results are appreciably better than with streptomycin and PAS. The administration of all three drugs simultaneously appears to add no further measurable benefit. A daily rather than a twice-weekly administration of streptomycin in conjunction with daily isoniazid appears to be the optimal regimen. This is universally recognized, at least tacitly, as it is the agreed-upon regimen for the most dangerous forms of tuberculosis, namely, the miliary and meningeal. In chronic pulmonary tuberculosis some prefer to use PAS with isoniazid in order not to risk the development of bacterial resistance to both of the two major drugs.—Editorial by C. Mushenheim, M.D., Isoniazid After Five Years, *A. M. A. Archives of Internal Medicine*, May 1957.

ANTIBODY RESPONSE IN VOLUNTEERS TO ASIAN INFLUENZA VACCINE

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Sally A. Anderson, B.S., Mary L. Luecking, B.S.
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The antibody response against Asian influenza virus was measured in 619 volunteer subjects who received Asian influenza vaccine or polyvalent vaccine in varying dosage at various time periods by the subcutaneous or intradermal routes. Blood was taken from each subject before and after the vaccination and was titrated for hemagglutination-inhibiting (HI) antibody. Pure egg-line Asian influenza virus strain A/Japan/305/57 in the fifth passage in eggs was used in these tests. When this strain of virus was used it was unnecessary to treat the serum with receptor-destroying enzyme or with potassium periodate. The vaccination was followed by marked rise in HI titer even when as little as 62.5 CCA units of virus were given. Some benefit from the second dose of vaccine was also demonstrated. Persons who received 200 CCA units developed as much antibody as did persons with proved cases of the disease. Reactions to the vaccine occurred in 18 subjects but were generally mild and inconsequential.

On May 22, 1957, this laboratory reported and later recorded [1] the occurrence in the Far East of a new strain of type A influenza which was strikingly different antigenically from strains recovered in previous years. Similar findings with viruses from the Far East were announced at about the same time by Drs. Isaacs and Andrewes in London and by Drs. Burnet and French in Melbourne. The marked shift in antigenic composition of the virus, the deficiency of antibody against it in the human population tested, and the rapid spread of the virus in the Far East with high attack rates indicated [1] the potential importance of the new virus as a major health problem to much of the world. Accordingly, strains of virus were furnished by this laboratory to the U. S. Public Health Service to send to the licensed vaccine manufacturers for purpose of vaccine production before the more widespread occurrence of the disease, and experimental lots of commercially prepared Asian influenza vaccine were received in this laboratory during June and July for study. These materials provided an unusual opportunity to measure the effectiveness of Asian influenza vaccine in stimulating antibody and, also, to gather data on antibody response against an influenza virus in a population which was essentially virginal insofar as experience with the principal antigens of the virus was concerned. This paper summarizes the findings in studies to measure the antibody response against Asian influenza virus in persons given Asian influenza or polyvalent vaccine in varying dosage at various time periods by the subcutaneous or intradermal routes. Additionally, data on the methodology for assay of Asian influenza antibody in human serums are presented.

Materials and Methods

Vaccines.—Three lots of monovalent Asian influenza vaccine prepared from strain A/Japan/305/57 [1] and one lot of old formula polyvalent influenza vaccine without the Asian strain were used in the present study. Lots 1 and 2 of Asian vaccine (Pitman-Moore), containing 185 and 160 chick cell agglutinating (CCA) units of virus per milliliter, respectively, were prepared by the eluate method. Lot 7-1225-103 of Asian vaccine (Lederle), containing 1,070 CCA units per milliliter, was purified by the Shraples technique, as was polyvalent lot 4397 (National Drug Company), which contained 200 CCA units each of A/Swine/1976/30, A/PR8/34, A'/PR301/54, B/Lee/40, and B/Great Lakes/1739/54.

Test Population.—The population under study consisted of 619 adult military or civilian personnel of Walter Reed Army Medical Center and of Fort Belvoir, Va. These persons were vaccinated during the period of July through September, 1957, and were finally bled not later than Oct. 4. This period was prior to widespread epidemic occurrence of Asian influenza in the United States and to the occurrence of any unusual prevalence of respiratory illness in this area. All persons were bled prior to and after vaccination, and the serums were stored frozen at −20 C until tested, up to four months later. The volunteers were interviewed for history of allergy to eggs, chickens, or chicken feathers, and those with a history of sensitivity were excluded from the study.

From the Department of Respiratory Diseases, Walter Reed Army Institute of Research.

Read in part at the Special Conference on Influenza, U. S. Department of Health, Education and Welfare, Aug. 27-28, 1957, Bethesda, Md.

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Laboratory Methods.—Titrations for hemagglutination-inhibiting (HI) antibody were performed by the standard test of reference technique [2] with use of human "O" red blood cells. Pure egg-line Asian influenza virus strain A/Japan/305/57 [1b] in the fifth passage in eggs was used routinely in the tests to measure Asian influenza antibody. The A/Swine/1976/30, A/PR8/34, A'/Hawaii/308/56, and B/IB1/50 strains of virus used to test for heterotypical antibody response to Asian influenza vaccine were standard stock viruses carried in our laboratory. Special tests with the animal-passage inhibitor-sensitive A/Japan/305/57 virus supplied by Dr. K. Jensen [3] were also carried out with use of virus passed in eggs one time in this laboratory after receipt (egg-passed, 4; ferret, 1; mouse, 3; and egg, 2). The cholera filtrate treatment of certain of the serums to remove nonspecific inhibitor was carried out by the method routinely used in our laboratory.[4] Treatment of the serum with potassium periodate to remove inhibitor was according to the method of Jensen.[3] Both cholera filtrate and periodate treatments were found to be excessively destructive of the low-titer Asian influenza antibody. Unless stated otherwise, serums tested for Asian A/Japan/305/57 antibody were not treated. Serums tested for antibody against other strains were treated with cholera filtrate. In the tests, all serum titers are expressed in terms of initial dilution. For comparison of these results with tests in which other workers present the final dilution, it will be necessary to divide the latter titers by 4.

Results—Methods for Assay of Antibody

It is well known [4] that human and animal serums contain nonspecific mucoprotein inhibitors which prevent hemagglutination and give false-positive results in the HI test. These substances may be removed from the serum by treating with the receptor-destroying enzyme [4] in filtrates of Vibrio cholerae or with potassium periodate,[3] a substance which oxidizes polysaccharides. Such treatment is useful where inhibitor-sensitive strains must be employed in the tests. However, the treatment is destructive of antibody in most serums irrespective of titer, and this effect is especially marked in serums of initially low antibody titer.

TABLE 1.—*Influence of Test Virus and of Serum Treatment on Assay of Asian Influenza Antibody in Human Serums (HI Antibody Titer Obtained with A/Japan/305/57 Virus*)*

	Egg Line			Egg-Ferret-Mouse Line		
	Untreated Control	Cholera Filtrate	Periodate	Untreated Control	Cholera Filtrate	Periodate
Nonvaccination, Cases						
1 Acute	0	0	0	160	0	0
Convalescent	10	0	0	160	10	20
2 Acute	0	0	0	160	0	10
Convalescent	20	10	10	160	40	40
Vaccination, Cases						
3 Prevaccination	5	0	0	160	5	5
Postvaccination	20	0	5	160	20	10
4 Prevaccination	0	0	0	80	0	0
Postvaccination	40	5	10	160	20	20

* Numbers are reciprocals of serum titers. 0 equals titer < 1:5, the lowest serum dilution tested.

TABLE 2.—*Titration of Asian Influenza Vaccine in Human Volunteers with Results Expressed as Geometric Mean HI Titer against Homologous Virus**

CCA Units		Mean HI Titer†			
		Prevaccination	Postvaccination		
1st Dose	2nd Dose		1st Dose		2nd Dose
1,000	1,000	2.8	30.0	28.4	46.9
1,000	500	2.6	25.5		32.5
1,000	250	5.0	30.1		37.9
750	750	1.9	17.6	23.4	34.4
750	500	2.1	22.1		32.3
750	250	1.8	35.5		44.8
500	500	3.9	26.8	20.8	27.5
500	250	2.8	16.8		27.2
250	250	2.0	11.8	12.5	19.9
250	125	2.5	13.3		20.5
125	125	1.3	7.8	6.2	10.1
125	62.5	0.9	4.8		7.5
62.5	62.5	1.2	9.3		11.7

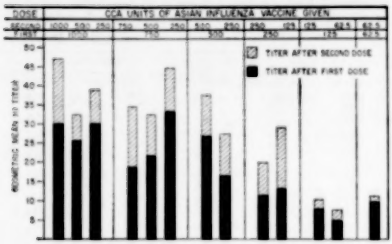
* See table 3 for numbers of volunteers per group. Subcutaneous route was used.

† Numbers are reciprocals of mean titers. Titers in serums before vaccination are largely, if not entirely, due to nonspecific inhibitor.

The egg-line Asian A/Japan/305/57 virus has shown evidence of being in Q phase,[1b] giving relatively low antibody titers in HI tests and being relatively insensitive to nonspecific inhibitor. Jensen [3] has recommended use of the egg-mouse-ferret passage of A/Japan/305/57 virus, which he reports as giving higher antibody titers than egg-line virus, while noting that the serums must be treated to remove the nonspecific inhibitors which are highly active against this strain.

Comparative titrations for Asian influenza antibody in treated and untreated serum pairs from patients with Asian influenza or from vaccinated volunteers were carried out using the egg line and egg-ferret-mouse line of A/Japan/305/57 virus. Representative findings in four cases, presented in table 1, show that significant increases in titer (fourfold or greater) were obtained in all persons when the untreated serums were tested with egg-line virus. After treatment with cholera filtrate or periodate, the titer of antibody in the second specimen was reduced and, in certain instances (cases 1 and 3), this was below the detectable level. Thus, the significant titer rises detected with untreated serums were allayed by treatment in two of the four cases (1 and 3). Untreated serums tested with Jensen's egg-ferret-mouse line of virus revealed the exquisite nonspecific inhibitor sensitivity of this strain which resulted in the obscuring of the true antibody titers. After treatment with cholera filtrate or periodate, the antibody levels became apparent. The titers were in the same range of magnitude as when the untreated serums were tested with egg-line virus.

However, inhibitor destruction was incomplete, and residual inhibitor was detected in the first specimen from two of the cases (2 and 3). Thus, there was no apparent advantage, under the conditions of the test and of the technique employed, in use of the egg-ferret-mouse line of virus which required serum treatment. Therefore, the egg-line virus without treatment of serum was routinely employed.


DOSE
CCA UNITS OF ASIAN INFLUENZA VACCINE GIVEN
1ST
2ND
1,000 500 250 750 500 250 500 250 250 125 125 62.5 62.5
1,000 750 500 500 250 250 125 62.5
GEOMETRIC MEAN HI TITER
TITER AFTER SECOND DOSE
TITER AFTER FIRST DOSE

Graphic presentation of findings in titration of Asian influenza vaccine in volunteers.

The egg-line A/Japan/305/57 virus has proved, for us, remarkably insensitive to nonspecific inhibitor, as measured by assay of serums collected prior to vaccination and to epidemic occurrence of Asian influenza in the United States. Thus, of the 619 pre-vaccination serums tested in this study, 357 (58%) showed a titer less than 1:5; 173 (28%), 1:5; 81 (13%), 1:10; and 8 (1%), 1:20.

TABLE 3.—*Titration of Asian Influenza Vaccine in Human Volunteers with Findings Expressed According to Increase in HI Antibody*

No. of Volunteers	CCA Units*		Increase in HI Antibody Following Doses							
			1st Dose				2nd Dose			
			2-Fold or Greater		4-Fold or Greater		2-Fold or Greater		4-Fold or Greater	
	1st Dose	2nd Dose	No.	%	No.	%	No.	%	No.	%
24	1,000	1,000	23	96	18	75	24	100	23	96
24	1,000	500	22	92	19	79	23	96	22	92
23	1,000	250	21	91	15	65	23	100	18	78
25	750	750	22	88	17	68	25	100	21	84
23	750	500	21	91	19	83	22	96	21	91
23	750	250	22	96	19	83	22	96	22	96
20	500	500	18	90	13	65	19	95	17	85
24	500	250	23	96	13	54	24	100	19	79
22	250	250	19	86	13	59	21	95	18	82
22	250	125	18	82	10	45	22	100	18	82
23	125	125	18	78	10	43	18	78	12	52
24	125	62.5	14	58	7	29	17	71	12	50
23	62.5	62.5	19	83	9	39	21	91	12	52

* Given by subcutaneous route.

Results—Antibody Response

Titration of Asian Influenza Vaccine in Volunteers.—Groups of 20 to 25 volunteers were vaccinated subcutaneously on two occasions three weeks apart with graded doses of Sharples-purified Asian influenza vaccine according to the schedule presented in table 2. The geometric mean titers before vaccination were low, as expected, for this "virginal" population and were due largely, if not entirely, to nonspecific inhibitor in the serums. There was a marked increase in the mean postvaccination HI titer for all doses of vaccine, even when as little as 62.5 CCA units of virus were given. It is also seen in table 2 and in the figure that the mean antibody titer following the first dose was roughly proportional to the CCA units of virus administered.

There was some benefit from the second dose of vaccine. The mean titer was increased, on the average, about one and one-half times, and the smaller of the second doses, in each group, appeared to provide about as much antibody stimulation as the larger. The antibody level achieved after a single injection of a given amount of virus was roughly comparable to that obtained when the same quantity of virus was given in two divided doses three weeks apart. For instance, a single dose of 1,000-CCA-unit vaccine gave a mean titer of 28.4, and in two 500-unit divided doses the level achieved was 37.5. Similarly, for 500-unit vaccine, the value was 20.8 compared with 19.9; for 250-unit vaccine, 12.5 compared with 10.1; and for 125-unit vaccine, 6.2 compared with 11.7.

TABLE 4.—*Homologous and Heterologous Antibody Response in Human Volunteers After Asian Influenza Vaccination, with Findings Expressed as Geometric Mean Titer**

CCA Units	Test Virus†	Prevaccination	After 1st Dose		After 2nd Dose	
			Mean	Mean Fold Rise	Mean	Mean Fold Rise
1,000 (24 volunteers)	A/Japan/305/57	2.8	30.0	10.7	46.9	16.8
	A/Swine/30	43.8	65.4	1.5	71.1	1.6
	A/PR8/34	101.0	113.0	1.1	117.0	1.2
	A'/Hawaii/302/56	6.6	10.4	1.6	11.3	1.7
	B/IB1/50	36.2	42.9	1.2	42.9	1.2
62.5 (23 volunteers)	A/Japan/305/57	1.2	9.3	7.8	11.7	9.8
	A/Swine/30	7.8	11.8	1.5	14.8	1.9
	A/PR8/34	69.3	71.4	1.0	73.6	1.1
	A'/Hawaii/302/56	5.0	6.5	1.3	6.8	1.4
	B/IB1/50	43.1	47.1	1.1	47.0	1.1

* Numbers are reciprocals of mean titers.

† Serum aliquots tested for Asian (A/Japan/305/57) antibody were not treated. Aliquots tested for antibody against other strains were treated with cholera filtrate to remove nonspecific inhibitor.

There was a marked height of antibody response to vaccination varied markedly with dosage, conversion from the negative to the positive antibody status, as evidenced by a twofold or greater increase in titer, occurred in most persons given a single dose of 250 CCA units or more of Asian virus. Thus, as shown in table 3, from 82 to 96% of persons given this amount of virus developed antibody. Following a second dose of vaccine, at least 95% of the persons were converted to positive status. Vaccine in 125 or 62.5 CCA units generally gave a lesser rate of conversion. The effect of dosage on titer increase, as for mean titer, was reflected in the percentage of persons who developed a fourfold or greater titer

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rise. Viewed from this perspective, as from mean titer, there was a decided advantage in giving vaccine above the 125-CCA-unit potency.

Homologous and Heterologous Antibody Response in Volunteers to Asian Influenza Vaccine.—The early study of Asian influenza strains [19] showed that persons with Asian influenza infection occasionally developed an increased amount of antibody against prototype A viruses of prior "vintage." This indicated the existence, in Asian influenza virus, of antigens in common with earlier type A strains. The extent of this relationship was measured, in the present study, by tests for heterologous antibody response in volunteers after vaccination with Asian influenza vaccine in large (1,000 CCA) or small (62.5 CCA) unit dosage. Tables 4 and 5 summarize the findings in terms of mean titer rise or of percentage of persons responding to homologous and heterologous virus. There was a small but definite increase in antibody against the A/Swine and A'/

TABLE 5.—*Homologous and Heterologous Antibody Response in Volunteers to Two Doses of Asian Influenza Vaccine, with Findings Expressed According to Increase in HI Titer*

CCA Units	Test Virus	Persons Showing Increase in HI Antibody: 2-Fold or Greater No.	2-Fold or Greater %	4-Fold or Greater No.	4-Fold or Greater %
1,000 (24 volunteers)	A/Japan/305/57	24	100	23	96
	A/Swine/30	14	58	2	8
	A/PR8/34	3	13	1	4
	A'/Hawaii/308/56	11	46	1	4
	B/1B1/50	6	25	...	...
62.5 (22 volunteers)	A/Japan/305/57	21	91	12	52
	A/Swine/30	12	52	...	...
	A/PR8/34	4	17	...	...
	A'/Hawaii/308/56	6	26	1	4
	B/1B1/50	4	17	...	...

Hawaii strains following vaccination. The extent was about the same for the 1,000 and 62.5 CCA-unit dosages. The lack of difference in response to the two dosages suggested that the rise was accomplished largely on a recall basis rather than from primary stimulation. The small antibody response to the type A/PR8 strain was no greater than that to influenza type B, and these rises may be due more to chance variation in the tests than to heterotypical crossing.

Comparison of Polyvalent with Monovalent Asian Influenza Vaccine on Antibody Response Against Asian Virus.—Early in the discussions of Asian influenza vaccination, the question was raised of the possible efficacy of old-formula polyvalent types A, A', and B vaccine in inducing antibody and/or protection against Asian influenza virus or of a reinforcement of the antibody response against Asian virus through incorporation of the heterologous strains in the vaccine. This was measured, in the present study, in volunteers given Asian or polyvalent vaccine alone or in combination. The findings summarized in table 6 revealed that there was no effect, either beneficial or adverse, in the administration in the same dose of Asian vaccine of 1,000 units of old-formula vaccine, compared with the response to Asian vaccine alone. Further, the administration of

TABLE 6.—*Comparison of Polyvalent with Monovalent Asian Influenza Vaccine According to Mean HI Antibody Response Against Asian A/Japan/305/57 Virus After Vaccination in Seventeen to Twenty-two Volunteers per Group*

1st Dose (CCA Units): Asian	1st Dose (CCA Units): Polyvalent	2nd Dose (CCA Units): Asian	2nd Dose (CCA Units): Polyvalent*	Mean HI Antibody Titer: Prevaccination	After 1st Dose	After 2nd Dose
185†	...	185	...	2.0	13.9	16.8
185	...	185	1,000	0.6	14.3	14.2
185	...	...	1,000	2.4	13.4	12.9
160‡	...	160	...	0.2	6.0	11.4
160	1,000	160	1,000	0.6	8.3	13.6
160	1,000	160	...	1.4	8.6	8.8

* Old-formula lot no. 4297 (National Drug Company), containing 300 units each of A/Swine/1976/30, APR8/34, A'/PR/308/56, B/Lee/40, and B/Great Lakes/1739/54.
† Lot 1 (Pitman-Moore).
‡ Lot 2 (Pitman-Moore).

polyvalent vaccine in the second dose did not increase the antibody response evoked by the initial injection of Asian vaccine alone.

Comparison of Subcutaneous with Intradermal Routes of Administration of Asian Influenza Vaccine.—Studies carried out initially by Van Gelder and co-workers [5] and later by others [6] have shown generally that the antibody response following injection intradermally of one-tenth the subcutaneous dose of influenza vaccine induced as good an antibody response as did the full amount given subcutaneously. Such response was measured with vaccines containing virus strains with which the

TABLE 7.—*Comparison of Subcutaneous with Intradermal Route of Injection of Asian Influenza Vaccine on Mean Antibody Response After Vaccination*

Vaccine	Route	CCA Units/Dose	Mean HI Titer*: Prevaccination	After 1st Dose	After 2nd Dose
Lot no. 1†	Subcutaneous	185	0.42	6.71	10.6
	Intradermal	23	1.35	8.45	12.9
	Subcutaneous	185	2.05	11.8	...
	Intradermal	18.5	...	...	14.3
Lot no. 2†	Subcutaneous	160	0.18	6.01	11.4
	Intradermal	16	0.37	4.53	10.1
Lot no. 7-1225-163‡	Subcutaneous	500	0.43	11.9	29.6
	Intradermal	50	0.29	10.7	19.1

* Numbers are reciprocals of geometric mean titers.
† Pitman-Moore.
‡ Lederle.

population had prior experience. The present study conducted with Asian influenza vaccine of 160 to 500 CCA-unit level in an essentially "virginal" population agreed with the earlier findings in experienced groups. It is seen in tables 7 and 8 that the mean antibody titer following vaccination and the percentage of persons showing twofold, fourfold, or greater postvaccination increase in antibody

after intradermal injection of one-tenth or one-eighth the subcutaneous dose was about the same as obtained when the full amount (1 ml.) was given subcutaneously.

Antibody Response to Multiple Injections of Asian Influenza Vaccine.—Volunteers were given two injections subcutaneously two weeks apart of 185 or 160 CCA units of Asian vaccine followed by an additional dose six weeks after the second. Tables 9 and 10 show that the antibody response to Asian virus was increased by the second and the third dose above that achieved initially by the single injection alone. The response to the third dose, given six weeks after the second, was not sufficiently great to suggest an anamnestic or booster effect. There was a small but measurable decline in antibody during the six-week period after the second dose of vaccine.

Vaccine Reactions.—Reactions to vaccination were minimal and inconsequential. Among 91 persons who received 1,000 CCA units of Asian vaccine subcutaneously, only 18 (20%) showed mild reactions; these were characterized by local soreness of several days' duration at the injection site, temperature up to 102 F (38.8 C) for three or four hours, and mild malaise for a similar period, beginning four to eight hours after the vaccination. The 750-unit vaccine gave fewer reactions (14%), and only 5% of persons who received 500, 250, or 125 units of vaccine developed a noticeable reaction. A half-day loss from duty was recorded for one person who received a 1,000-unit vaccine. All persons given vaccine intradermally developed erythema at the injection site, usually no greater than 4 cm. in diameter. A few persons showed induration 4 cm. or greater in diameter in addition to erythema. These individuals were not vaccinated further and were excluded from the study. The reactions usually developed on the second to fourth day after injection and subsided in a day or two. There was no anaphylactic reaction among any of the volunteers, but two individuals did develop a mild generalized urticarial reaction which began two or three days after vaccination.

Comment

The technique employed for assay of influenza antibody, whether for vaccine assay or for diagnostic purpose, should be simple and should provide definitive quantification of antibody without serum treatment procedures which are destructive of antibody. These criteria were met in the present study by use of egg-line A/Japan/305/57 virus, which was remarkably unaffected by inhibitor and which was kept in low egg-passage (five or less) to maintain this desirable property. Only one other Asian influenza strain, A/Formosa/313/57, [15] recovered in the initial study,[1] exhibited such nonsensitivity to inhibitor.

Definitive information is presently lacking relative to what exact level of HI antibody is protective against Asian influenza. However, examination of convalescent serums from 171 serologically proved cases of Asian influenza revealed a geometric mean titer of 1:14.3, and it is reasonable to assume, therefore, that this general level of antibody should be protective. In the present study, vaccine in the approximate 200-CCA-unit level usually induced at least this amount of antibody after a single subcutaneous injection. It is not surprising, therefore, that the standard 200-CCA-unit vaccine, according to present findings, was highly effective in preventing Asian influenza in the pandemic.[7] The use either of greater than 200 units of virus in the initial vaccine dose or of one or two added injections of vaccine consistently elevated the antibody titers. This suggested a margin of benefit providing immunity of probably longer duration in a greater proportion of individuals than achieved by the single 200-unit dose alone. There was no evidence of the anamnestic or recall reaction in volunteers when the vaccine doses were administered from two to four weeks apart. It is probable that a far greater time period between injections will be required to achieve this effect.

The lack of significant benefit of old-formula polyvalent (A, A′, and B) influenza vaccine either in inducing antibody against Asian virus or in en-

TABLE 8.—*Comparison of Subcutaneous with Intradermal Route of Injection of Asian Influenza Vaccine on HI Antibody Titer Increase Against Homologous Virus*

No. of Volunteers	Vaccine	Route	CCA Units/ Dose	Persons Showing Increase in HI Antibody							
				After 1st Dose				After 2nd Dose			
				2-Fold or Greater		4-Fold or Greater		2-Fold or Greater		4-Fold or Greater	
				No.	%	No.	%	No.	%	No.	%
22	Lot no. 1*	Subcutaneous	185	18	82	8	36	21	95	14	64
30		Intradermal	23	22	73	10	33	29	97	17	57
14		Subcutaneous	185	12	86	7	50	...	...	...	...
		Intradermal	18.5	...	...	...	...	14	100	8	57
21	Lot no. 2*	Subcutaneous	160	18	86	9	43	20	95	13	62
19		Intradermal	16	14	74	7	37	19	100	12	63
20	Lot no. 7-1225-161†	Subcutaneous	500	16	80	11	55	20	100	19	95
26		Intradermal	50	23	96	21	81	26	100	25	96

* Pitman-Moore. † Lederle.

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hancing the antibody response to Asian vaccine is not surprising in view of the novel antigenic composition * of the Asian influenza strain. The stimulation, on the other hand, of a slight but detectable amount of antibody against swine or A′ virus by Asian influenza vaccine, supports the concept presented earlier [10] that the Asian virus does not consist entirely of antigens created *de novo* with no relationship to viruses of the past. Instead, it appears that the principal hemagglutinating antigens of the Asian virus are strikingly different from the principal antigens of A or A′ strains. Found in common are minor hemagglutinating components and the group-specific "soluble" complement-fixing antigen.

The failure of the old-formula vaccine to induce significant antibody against Asian virus suggests strongly that the former material should be without significant effect in preventing Asian influenza, even though such has not been indicated in the preliminary findings in trials carried out at Great Lakes, Ill.[7] Final judgment in this important aspect of the influenza immunization problem must await the definitive data with critical appraisal.

The present findings in tests of the 0.1-ml. dose given intradermally have shown an effect essentially equal to that obtained with the full 1-ml. subcutaneous dose, in terms both of mean antibody titer and of the rate of conversion of individuals from the negative to the positive antibody status. The former method presents considerable advantage in conserving vaccine during the period of critical need and in reducing the cost for vaccination. However, because of the uncertainty of actual infiltration into the skin in mass immunization programs and because there are no data from field evaluations to prove the efficacy of vaccine administered dermally in preventing illness, the 1-ml. amount given subcutaneously is preferred for routine purpose. Evaluation of the 0.1-ml. dermal dose under field conditions seems highly desirable in the not distant future to provide for handling of the next pandemic in which the same critical shortage of vaccine is likely to exist but which may not present the same benign features of the present disease.

TABLE 9.—*Mean Antibody Response to Multiple Injections of Asian Influenza Vaccine*

		Mean HI Titer*	
		Lot No. 1† (24 Volunteers)	Lot No. 2‡ (21 Volunteers)
	Week		
Prevaccination	...	1.3	...
After Dose 1	2	11.5	2.9
After Dose 2	4	15.8	6.6
Before Dose 3	8	14.4	4.2
After Dose 3	10	21.0	9.1

* Numbers are reciprocals of mean HI titers.
† Pitman-Moore; 185 CCA units of vaccine were used.
‡ Pitman-Moore; 160 CCA units of vaccine were used.

Summary

Studies were conducted to measure the antibody response against Asian influenza virus in 619 volunteers given monovalent Asian influenza vaccine alone or combined with old-formula polyvalent (A, A′, and B) vaccine, according to chick cell agglutinating (CCA) units given, number of doses, time-period between injections, and route of vaccine administration. There was some advantage in administering one or two additional injections over a single dose in terms of increased mean antibody level. The level of antibody achieved after a single dose of vaccine, however, was roughly the same as when given in two divided doses three weeks apart. Although the height of the antibody response varied according to dosage, most persons who received vaccine in the 62.5 or greater CCA-unit range showed a detectable response. Persons who received vaccine in the approximate 200-CCA-unit level developed as much antibody as did persons with proved cases of the disease. Asian vaccine administered in a 1,000 or 62.5 CCA-unit amount induced a small but measurable antibody response against type A/Swine/30 and type A′/Hawaii/303/56 viruses, indicating the existence of common antigens between the Asian, A, and A′ agents. However, the old-formula A, A′, and B vaccine neither induced detectable antibody to Asian virus nor enhanced the Asian antibody response when added to the Asian vaccine. Asian vaccine given in a 0.1-ml. amount intracutaneously induced essentially the same antibody response in volunteers as the full 1 ml. dose given subcutaneously. Reactions to the vaccine were minimal and usually inconsequential, even when 1,000 CCA units were given. Definitive assay of Asian antibody in serums of the volunteers was accomplished in the tests without necessity for serum treatment by use of the relatively noninhibitor-sensitive egg line of A/Japan/305/57 virus.

TABLE 10.—*Homologous Antibody Response to Multiple Injections of Asian Influenza Vaccine with Results Expressed According to Cumulative Increase in HI Titer*

		Volunteers Showing HI Antibody Increase			
		Lot No. 1* (24 Volunteers)		Lot No. 2† (21 Volunteers)	
Dose	Increase	No.	%	No.	%
1st	2-fold or greater	22	92	12	57
	4-fold or greater	15	63	7	33
2nd	2-fold or greater	23	96	16	76
(2 wk. after 1st dose)	4-fold or greater	18	75	11	52
3rd	2-fold or greater	23	96	18	86
(6 wk. after 2nd dose)	4-fold or greater	21	88	15	71

* Pitman-Moore; 185 CCA units of vaccine were used.
† Pitman-Moore; 160 CCA units of vaccine were used.

Major S. Vivona, M.C., U. S. Army, made the statistical computations.

Lots 1 and 2 of Asian vaccine were furnished by Dr. Samuel Bozeman of Pitman-Moore Company, Indianapolis; lot 7-1225-103 was supplied by Dr. I. S. Danielson of Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.; and lot 4397 was supplied by Dr. A. E. Bolyn of the National Drug Company, Philadelphia.

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PANDEMIC INFLUENZA IN 1957

REVIEW OF INTERNATIONAL SPREAD OF NEW ASIAN STRAIN

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The principal events of the pandemic of Asian strain influenza can be discussed and studied in chronological form, although it is unlikely that the point of origin will ever be precisely located. The disease was first reported in late February, 1957, in China. From established foci in countries along the eastern fringe of Asia the disease spread to many new areas in May. North America, northern South America, and Europe experienced widespread Asian strain influenza epidemics before the month of September was over.

It would seem that the most important timing factor for epidemic occurrence in the equatorial regions was the presence or absence of the virus in sporadic cases. In regions where seasons are well marked the situation was much more complex. In the regions far from the equator, greater crowding and more opportunities for close contact are more likely to exist in fall and winter. The apparent shortening of time necessary for world-wide spread in the most recent pandemic reflects the speed and extent of modern travel.

"The special characteristics of influenza pandemics are their wide and rapid extension, their high attack rates, and their great effects upon general mortality rates." In this way Wade Hampton Frost defined pandemic influenza.[1] In all respects the new A/Asian strains of influenza virus have fulfilled these requirements to produce the second influenza pandemic of this century and the first since the development of the science of virology. Attack rates have been high in many parts of the world, and mortality rates have been affected strikingly, although they do not approach those of the 1918-1919 pandemic. In little more than six months after the disease jumped from the mainland of China to Hong Kong, Asian strain influenza spread to virtually every country and corner of the world. It is apparent, furthermore, that the virus was disseminated in many of these countries even more rapidly—perhaps in a period of only three or four months, although conditions were not always ideal for the immediate occurrence of epidemic disease.

This review of the international spread of Asian strain influenza was compiled from information received by the Influenza Surveillance Unit of the Communicable Disease Center, U. S. Public Health

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Service.[2] Much of the information is preliminary and, in certain cases, fragmentary in nature. Many months and perhaps several years will elapse before a complete and detailed international history of the pandemic can be written. The discussion of the principal events of the pandemic follows, in general, a chronological form.

February and March—Beginning of a Pandemic

It is unlikely that the point of origin of the new strain of type A influenza will ever be precisely located. It is evident, however, that the first outbreaks of the pandemic occurred in China.[3] The disease was reported in late February in Kweichow province, near Kweiyang. In early March Yunan province was affected, and, by the middle of the month, epidemic influenza was occurring in many parts of China. Asian strain viruses were isolated in Peking, Chang Chia-Kow, Lo-Yang, and Changchun. An isolate obtained from Dr. Tang Fei-Fan was examined at the WHO world influenza center later in the year and identified as a typical Asian strain.

April

In early April epidemic influenza appeared in Hong Kong, and soon thereafter new epidemics were reported in Taiwan, Borneo, and Singapore. By the end of the month the new strain had been introduced into Japan. Laboratory characterization of virus isolates obtained from several of these early epidemics resulted in a world-wide alert for a possible pandemic.[4]

Hong Kong.—The first patients with Asian strain influenza to arrive in Hong Kong were probably refugees from Communist China. The disease, which was epidemic by the week ending April 12, was noted to be mild, characterized chiefly by fever, headache, myalgia, malaise, and sore throat. The mortality was very low; the over-all attack rate was about 20%. The new strain was isolated from a number of patients before the epidemic subsided in mid-May.

Singapore.—In mid-April influenza appeared in Singapore, introduced probably by ships. Clinically the disease was similar to that in Hong Kong, and the mortality rate apparently was low. Prof. J. H. Hale is quoted in the World Health Organization Influenza Report, July 3: "We can only trace about 24 deaths in Singapore attributable to flu. These were in young children and were the result of complications such as bronchopneumonia. Two cases showed interstitial pneumonia and we were able to isolate the virus from the lungs. One significant fact worth mentioning is that the over-all reports of deaths in the city (from any cause) were much higher during the epidemic than at any other time."

Professor Hale described the Singapore Naval Base outbreak at an informal influenza meeting at the Fourth International Poliomyelitis Conference. The following information is from his report: The outbreak lasted 38 days in May and early June, with more than half the cases occurring between May 9 and 18. At the Singapore Naval Base, 3,383 of 18,391 persons became ill (attack rate 18.4%); 3,296 of the 17,145 Asians and 87 of the 1,346 Europeans became ill (attack rates 19.2% and 7.0% respectively).

Two hundred ninety-eight patients, all Asians, were hospitalized. There were 41 patients with complications among them, including 15 with pneumonia and 16 with bronchitis. Most of the hospital admissions were in the younger and older age groups, with relatively few young adults.

Taiwan.—Influenza moved to Taiwan, probably by both ship and air from Hong Kong, in late April. The epidemic, which lasted until mid-June, attacked an estimated 1,900,000 people of a total population of about 8 million. There was no marked increase in general mortality on the island. As in Hong Kong and Singapore, the Asian strain virus was isolated soon after it appeared on the island.

Borneo.—The next appearance, chronologically, of the new virus was in Borneo where the first cases appeared in the last week of April. A minor epidemic carried on into May, but details of its course are lacking.

Japan.—On April 25 a vessel from Hong Kong docked at Yokosuka, Japan, with a number of patients with febrile respiratory illness aboard, from whom the Asian strain virus was isolated. This first appearance of the disease in Japan did not, however, result in immediate spread to the general population nor did the occurrence of several cases at a U. S. Air Force base in early May. By late May, however, dissemination of the virus was extensive, for on June 1 the disease was reported to be "all over the country." On that date schools were closed because of epidemic influenza in 18 prefectures, of which 15 were on the main island. The epidemic appeared to affect children primarily; the disease was mild; and the mortality was very low. No data on excess mortality are available at this writing (December, 1957). The new strain was isolated from patients during May and June. The epidemic peak occurred in mid-June, and by mid-July the disease had virtually disappeared.

May

From established foci in countries along the eastern fringe of Asia and from major shipping centers, particularly Hong Kong and Singapore, the disease spread with facility to many new areas including Malaya, Cambodia, the Philippines, Guam, Okinawa, India, and Indonesia. In addition, minor outbreaks were reported in Australia and on several steamships en route to San Francisco. Opportunities for transmission of the disease to new countries by aircraft and ship passengers and crewmen were innumerable, and many such transmis-

sions undoubtedly went undetected. Quarantining was of little avail in preventing the spread of the disease.

Malaya.—Because of the proximity of Singapore and Malaya, it is not surprising that influenza appeared in Malaya soon after the Singapore epidemic. The disease appears to have moved on land and by coastal vessels from south to north up the Malay peninsula. On May 8 the first evidence of an epidemic was noted in Johore, and by May 12 the first cases were appearing in the northernmost states. In general, it was noted that the poor were attacked before the more well-to-do and the urban dwellers before the rural people. Attack rates were higher among Asians than non-Asians. Capt. R. E. Shope, of the Walter Reed Army Institute of Research, reported that the attack rate approached 100% among Asian employees at the Kuala Lumpur Army Medical Research Unit, while the rate was much lower among the non-Asian personnel. The epidemic was reported to be at an end in the last week of July. The Asian strain was isolated in Malaya; the clinical picture was essentially the same as in other areas affected.

Philippines.—It is likely that contact with Hong Kong resulted in the introduction of the disease into the Philippines. A few cases were noted in the first week of May, but the epidemic onset occurred about May 18. For the peak epidemic week in Manila, that ending May 25, the excess mortality over that of the comparable 1956 week was 498 (that is, 693 deaths from all causes compared to 195 in 1956).[8] It was noted that for all ages the combined total mortality was 2.4 times what would have been expected, based on the May, 1956, experience. The greatest difference in mortality occurred in the 5-to-9-year age group, but every age group showed a substantial increase. The end of the Manila epidemic occurred in mid-June, but epidemic influenza continued in other parts of the country until late July.

Sarawak and North Borneo.—Influenza-like illness became epidemic in Sarawak and North Borneo in mid-May. The disease may have spread to them from the earlier epidemic in Borneo. By late July Sarawak was epidemic-free, and North Borneo reported marked decline. Mortality in both countries was very low.

Australia.—While substantial epidemics were appearing to the north, Australia experienced a series of local outbreaks. In early May, a sharp outbreak occurred in Victoria secondary to cases among passengers arriving by air from Europe via Singapore. Some 200 cases were reported, but the outbreak did not spread. The Asian strain virus was isolated. At Cairns, about the same time, a small outbreak occurred secondary to cases off a ship from Singapore. Again the Asian strain was isolated. In mid-May, under similar circumstances, cases appeared at Darwin. Australia reported few cases during June, but, on July 18, an outbreak was reported in New South Wales. During July a number of other areas experienced sporadic or local outbreak influenza, but marked spread did not occur until August, when many states (and Tasmania) were heavily affected. High industrial absenteeism was noted in some areas. By early September every state had been significantly involved, and the disease was everywhere on the decline.

Guam.—In the first week of May in Guam a number of influenza cases were noted in recent arrivals from the Philippines. By the third week an epidemic was in progress. At this time a ship transporting laborers from the Philippines brought more than 300 additional cases to Guam. This ship was accused originally of introducing the virus to the island. During June the epidemic continued, the disease attacking about 4,000 civilians and 1,000 military personnel. The two-month epidemic was reported to be waning only in the second week of July. The over-all attack rates were at least 14% among civilians and 4% among military personnel. Several deaths due to pneumonia were recorded.

Cambodia.—Asian strain influenza returned to the mainland (excluding the Malay peninsula) about May 20, when it appeared in Cambodia. A sharp epidemic ended about July 1.

India.—On May 17 a ship from Singapore arrived in India with 44 patients with active cases aboard to launch the westward movement of the disease. Madras, on the east coast, was stricken first. On May 1 Bombay, on the west coast, reported its first cases (some 500), presumably also secondary to ship or aircraft transmission from Singapore. Calcutta did not report cases until June 2 but five days later noted 1,270 cases with 36 apparently associated deaths. Influenza was epidemic in New Delhi by mid-June, and soon thereafter the entire country was involved. Millions of cases had been reported by late July. Mortality rates apparently did not remain at the high level of the early Calcutta report. In late July influenza was still widespread in India and spreading in some provinces. The epidemic had ended or sharply declined in all states except Himachal Pradesh by the final week of September.

Indonesia.—Within a few days of the onset of influenza in India, Sumatra and Java also became involved. During the first half of June influenza was epidemic in Djakarta and by the third week throughout the main and outlying islands. By the latter part of June there were reported 6 million cases in Indonesia with an estimated population of 78,000,000. In late July influenza was declining throughout the country, but all areas were not epidemic-free until the end of August.

June

During June more than 20 countries in various areas of the world were affected for the first time. Early in the month Vietnam, Laos, Thailand,

Burma, West Pakistan, and Bahrein reported onsets of influenza epidemics. Several confirmed cases of Asian strain infection reached the Netherlands from Indonesia by ship and aircraft at about this time. During mid-June East Pakistan and Korea noted epidemic onsets, and outbreaks of influenza-like illness were reported in Czechoslovakia. Several ships bound for England, Hawaii, and the United States experienced outbreaks which had not entirely subsided by the time of arrival in these countries. Later in June, frequent new introductions and localized outbreaks were reported from the United States and Alaska. An outbreak in Romania at this time was later confirmed as having been caused by the Asian strain. Ceylon and Netherlands New Guinea noted onsets of epidemics at the end of the month. The most important event of the month was the well-defined westward spread of epidemics across the Middle East, from West Pakistan to the Red Sea. During the last third of June, Iran, Iraq, Saudi Arabia, Kuwait, Yemen, and Aden were affected, roughly in that order. At the end of the month the disease jumped the Red Sea to Eritrea and on to Mozambique on the east coast of Africa. Moslem pilgrims bound for Mecca are known to have played a role in the westward spread of the epidemics.

In the remainder of this review, detailed discussions will be presented for only a few of the countries reporting new epidemics each month.

Thailand.—Influenza was very active in Thailand during June and early July. The onset of the disease in Bangkok occurred about the first of June. The northward spread by land seen in the Malay peninsula may have carried the disease into Thailand. Figures for a six-week period in June and July (table 1) demonstrate clearly the early urban character of the disease, followed by a later spread to rural areas (as noted, also, in Malaya).

Netherlands.—On June 4 a passenger with a febrile respiratory illness arrived in the Netherlands from Djakarta by plane. Asian strain virus was isolated from his throat washings. This was the first known case of Asian strain influenza to reach Europe. Later in June and in early July, several ships arrived in Amsterdam and Rotterdam from the Orient with patients with active cases of influenza. By June 16, spread had begun to occur; first in a girls' institute near Amsterdam, where the attack rate was about 30%; then, in schools in the Amsterdam area, in two of which the attack rate was 60%; and finally, after July 1, sporadically in adults in Amsterdam and Utrecht. Sporadic and local outbreak influenza persisted throughout the summer. Generalized epidemic influenza did not occur until mid-September, when many other European countries also experienced epidemic onsets.

West Pakistan.—On June 6 Karachi reported a few cases in recent arrivals from Singapore and Bombay. Five days later, Lahore, far to the north in the Punjab but in contact with Karachi by rail and air, reported about 50 cases. In the third week of June, Karachi reported 13,000 cases, and, by the end of the month, a major epidemic was in progress. In the third week of July a marked decline in new cases occurred in Karachi, but rural spread continued. The epidemic did not end in West Pakistan until late September.

England.—London and Bristol reported confirmed Asian strain influenza in crewmen of ships returning from the Orient during mid-June. There were, however, few secondary cases. A British troopship from Hong Kong reached England at about this time with a history of 130 cases during the voyage. The ship had made stops at Cape Town and Durban, South Africa, where it had been quarantined, and in the Canary Islands.

Iran.—Abadan and Khorramshahr, ports on the Persian Gulf, reported 68 influenza cases on June 24, primarily among sailors. Four days later cases were reported among army personnel in Teheran and, by July 21, 25% of the 2,000,000 population of Teheran had been reported ill. By late July the country-wide attack rate was reportedly 30 to 35%

TABLE 1.—*Incidence of Influenza in Bangkok and Procincial Areas of Thailand*

Weekly Period	Bangkok	Provinces
June 4–8	50,000	16,000
June 9–15	3,000	178,000
June 16–22	1,000	180,000
June 23–29	less than 1,000	140,000
June 30–July 6	less than 1,000	140,000
July 7–13	92	91,000

with the epidemic still in progress and spreading. Mortality was very low, and less than 5% of those affected were developing pulmonary complications.

Saudi Arabia.—Jidda, the port for Mecca, first reported influenza in the last week of June. At this time many Moslem pilgrims were arriving in these cities. In an epidemic in Dhahran, peaking in early July, there was a high attack rate, both among Arabian oil company employees and overseas personnel. The Dhahran epidemic declined rapidly. Yemen, Kuwait,[6] and Aden also reported onsets of epidemics at this time. In Aden the attack rates were very high and it was calculated[7] that the excess mortality in 1957 over the comparable period in 1956 amounted to about 200 deaths—one death for every 350 cases in Aden. Pneumonic complications were frequent, and a number of bacterial organisms were incriminated, although some of the pneumonia cases were apparently nonbacterial.

July

In the first two weeks of July many countries of the Middle and Near East reached their epidemic peaks. In addition, Syria, Afghanistan, Jordan, and Lebanon became involved. In Jordan, Moslem pilgrims stricken with influenza were known to have passed through Amman shortly before the onset of

the epidemic. Further spread in the eastern half of Africa occurred at this time as South Africa, the Sudan, and French Somaliland reported epidemics. Influenza appeared dramatically in South America, without any proved sources of introduction, early in the month. Bolivia, Ecuador, and Panama reported epidemics at this time. In the second half of July outbreaks were reported from such diverse places as Greenland, New Zealand, Newfoundland, Mauritius, southern Italy, and widely scattered islands of the southern and western Pacific region. Chile, Colombia, Mexico, and Egypt reported sporadic cases and outbreaks of influenza toward the end of the month. Slow dissemination of the virus continued in the United States, England, the Netherlands, and undoubtedly in other countries of the Northern Hemisphere. This dissemination was characterized by sharp outbreaks of characteristically mild illness in closed population groups, primarily military installations, institutions of various types, and children's camps. During July declines from epidemic peaks occurred in Thailand, Laos, Vietnam, Burma, and Korea.

Ecuador.—In the second week of July approximately 5,300 cases of influenza-like illness were reported among children of 85 Ecuadorian schools. The Asian strain virus was isolated from a number of these cases. The epidemic continued into August, attacking an estimated 30% of the general population before it came to an end.

Bolivia.—Influenza appeared in La Paz on July 7. By the end of the month there had been some 200,000 cases in La Paz alone (population 375,000). The disease was mild, with few complications and very low mortality. Attack rates were extremely high in the younger age groups. In the group aged 0 to 6 years, the attack rate was 80%; 7 to 15 years, 91%; 16 to 59 years, 49%; and over 60 years, 7%.[24]

South Africa.—In the latter part of July, Cape Town, Durban, and Johannesburg were heavily invaded by influenza. By Aug. 6 the disease was spreading through the country districts. It was noted that school children were particularly affected in Durban, but, in general, the highest attack rates were noted among African miners who live in crowded compounds. Asian strain influenza was confirmed in a number of outbreaks. By Sept. 1, at least 200,000 cases had been reported with very few influenza-associated deaths.

Chile.—On July 22 a few influenza-like illnesses were noted for the first time in Santiago. A few days later Valparaiso was also involved. As major epidemics developed in these cities, many other Chilean communities reported outbreaks, and, in mid-August, when the epidemics had declined in the largest cities, influenza was widespread in the rural areas. A country-wide decline was apparent only in early September. An influenza study group of the United States Armed Forces Epidemiological Board was present in Chile during the epidemic period. Dr. F. M. Davenport, of this group, summarized the epidemiological data as follows: ". . . it would appear that a widespread outbreak has occurred involving between 25 and 30% of the population. The attack rate probably follows the usual pattern being highest in childhood. During the epidemic the death rate (from all causes) has doubled. The extremes of life have accounted for the greatest proportion of the deaths. Pneumonia, complicating or as a sequel to influenza, probably accounts for a large share of the increased mortality."

Mexico.—The earliest influenza reports for Mexico came, in late July, from Tijuana, just south of San Diego, Calif., where numerous cases had already been confirmed among both military and civilian groups. At the end of the month a mild epidemic was apparently under way in Mexico City. Asian strain confirmations were made in a school epidemic near the city. During August epidemic influenza persisted in scattered form throughout the country, but there was apparently no major widespread epidemic as seen in Chile. Mexico was reported to be epidemic-free by the end of September.

Egypt.—Asian strain influenza probably entered Egypt soon after the middle of July. By the end of the month, 1,800 cases were reported and an epidemic was under way in Cairo. Asian strain influenza was identified. Epidemic decline was evident throughout the country in early September.

Italy.—In late July a U. S. destroyer arrived at Leghorn from East Africa with patients aboard with clinically diagnosed influenza. The ship was quarantined, and apparently no cases occurred ashore. Early in August, however, 100 cases of influenza suddenly appeared among the NATO headquarters personnel (primarily Italians and Americans) at Naples. Italy was only the fifth European country to become involved in any way, so far as we know, by the pandemic.

August

By the end of August epidemic influenza had disappeared from most countries of eastern and western Asia. Decline was marked in Australia, after slow spread of the disease throughout the country. In New Zealand, however, the epidemic peak was not reached until early September. In southern Europe, Central and South America, and parts of Africa, epidemics were on the upswing or in full progress during the month. In Africa, Ethiopia, Tanganyika, and Kenya, on the east coast, reported epidemics in the first third of the month. The disease appeared on the west coast, in French West Africa, Senegal, Nigeria, and the Ivory Coast, several weeks later. The interior of the continent remained apparently influenza-free at month's end. Many new islands of Oceania were affected during August, and, in the Caribbean, Puerto Rico noted the onset of a major epidemic late in the month. Trinidad, reporting a localized

mild outbreak among military personnel, was apparently the only other Caribbean island affected before September. In southern South America, Argentina reported the onset of an epidemic early in the month, which almost rivaled that which occurred almost simultaneously in Chile. As the weeks passed, many other countries became involved, including Peru, Uruguay, southern Brazil, and British Guiana. In Central America, Costa Rica and El Salvador described sharp epidemics of Asian strain influenza, with high attack rates, which reached peaks early in September.

In August both Europe and North America reported their first true epidemics due to the Asian strain. The first community epidemics in the United States occurred in early August in several southeastern states. The sporadic introductions and outbreaks of July in Italy resulted in a major countrywide epidemic in late August and September. Schools were closed in Rome and other cities; a considerable number of influenza-associated deaths had been reported by Oct. 1.

Oceania.—During July and August many islands of the Pacific experienced intense epidemics of Asian strain influenza. Fiji (reporting a 600-person epidemic), Tongo (875 cases), the Gilbert and Ellice Islands (783 cases), Western Samoa (845 cases), and New Hebrides (396 cases) were among these. Guam reported that at least 4,600 cases had occurred on the island since the first appearance of the Asian strain there. Less heavily affected islands, but nevertheless reporting outbreaks, included Nauru, New Caledonia, the Solomon Islands, and the islands of the United States Trust Territory.

Argentina.—The epidemic in Argentina began in Mendoza province, spread north to Salta and Jujuy, then south to Cordoba and Buenos Aires. The peak for the nation was reached about Aug. 25. At that time at least 400,000 persons out of a population of some 18 million were ill. By the first week of September the number of cases had dropped to 200,000. The illness was mild and complications were rare. Absenteeism reached 25%, however, in some industries—twice normal for the winter season. No factories were shut down. School absenteeism was also marked, at least in Buenos Aires.

Uruguay.—In Uruguay, which also experienced a major epidemic during late August and early September, the over-all attack rate for the country was considered to be close to 40%. School and industrial absenteeism varied between 30 and 45%.

Peru.—The first epidemics in Peru were reported from Cuzco and Puno, in the southern highlands near Bolivia, in late August. Spread north to Lima had occurred by early September, and the whole country was involved during the month. A number of schools were closed in Lima because of high absenteeism, and 20% absenteeism was recorded in some Lima industries during part of the epidemic period.

El Salvador.—In El Salvador, where a vigorous epidemic reached its peak between Aug. 26 and Sept. 1, absenteeism among office workers in San Salvador was reportedly between 15 and 20%. Industrial absenteeism was also increased, but estimates of the increase are not available at this time.

September

The Middle East and eastern Asia were essentially free of epidemic Asian strain influenza by the end of September. Israel, isolated from contact with the other countries of the Middle East, had remained unaffected during the summer months while epidemics raged on all sides. The onset of an epidemic was noted in Israel only in late September and early October when surrounding countries were nearly free of the disease.

North America, northern South America, and Europe experienced widespread Asian strain influenza epidemics before the month was over. In Europe, influenza continued to sweep through Italy and appeared in epidemic form in Turkey, Cyprus, Sicily, Germany, and Bulgaria. Outbreaks and Asian strain virus isolations from sporadic cases were reported for the first time from Switzerland, Belgium, Poland, Greece, France, and Portugal. England and the Netherlands experienced increases in weekly case reporting after several months of sporadic outbreaks and cases.

In northern South America, French Guiana, Surinam, Venezuela, and the northern two-thirds of Brazil were in the midst of epidemics during September, while the countries of southern and western South America were reporting that their epidemics were at an end. In Central America and the Caribbean, Honduras, Guatemala, the Bahamas, and the Virgin Islands reported epidemics and outbreaks early in the month. Trinidad continued to experience local outbreaks. Puerto Rico was swept by a major epidemic during the month. In the United States and Canada, school openings were soon followed by rapid spread of epidemic influenza after a summer of increasingly frequent local outbreaks and sporadic cases.

During September only Liberia joined the roster of African countries which experienced epidemic influenza. North Africa remained apparently unaffected, except for Egypt, and no reports were received of influenza in the interior of the continent.

Alaska.—The first epidemics of influenza in Alaska were recorded only in late September, although sporadic illnesses and outbreaks had been occurring in the Territory for several months. On Sept. 27, Barrow reported that 500 of the 950 residents had developed influenza during a short period of time. Nome reported more than 500 cases among a population of 1,876. Two influenza-associated deaths were recorded in Nome among those who were ill—one infant and one elderly person. The experi-

ences in these isolated communities demonstrate the high general attack rates that were noted in many areas of the world during the pandemic.

Canada.—The earliest reports of influenza in Canada came from Newfoundland, where several outbreaks occurred during August. Early in September passengers with influenza-like illnesses were known to have disembarked in Quebec City from ships arriving from England. Between Sept. 7 and 14 a confirmed Asian strain influenza outbreak occurred at a girls' camp near Doe Lake in Ontario. In mid-September unconfirmed outbreaks were also recorded in several other Ontario and Quebec towns and in Calgary, Alberta. On Sept. 26 a report was received of a large outbreak on Prince Edward Island. Nova Scotia and British Columbia also reported smaller outbreaks at this time. By early October epidemic influenza was spreading rapidly in Quebec, the Maritime Provinces, and Ontario. During the succeeding six to eight weeks the epidemic spread westward, involving all provinces.[27] The Northwest Territory and Yukon Territory were not swept with the same intensity as the provinces along the United States border.

Brazil.—Although the southernmost states of Brazil were invaded by Asian strain influenza during August, most of the rest of the country was not affected by the epidemic until the end of September. The great coastal cities recorded their first confirmed cases only in the first week of September. Rio de Janeiro reported the onset of a major epidemic in the last week of September, and by Oct. 2 the city had recorded an estimated 500,000 cases. The northernmost states of Brazil were apparently the last to be affected.

Germany.—The first outbreak of influenza was reported among United States military personnel in Mannheim about Aug. 15. Soon thereafter, Asian strain virus was isolated from an outbreak at a German Army camp near Kassel. By mid-September the Ruhr had been hit by epidemic influenza, further Asian strain isolations had been made, and several influenza-associated deaths had been reported. Some parts of western Germany were reporting 50% attack rates in the general population. United States military personnel were heavily attacked during the month. An epidemic peak was reached in West Germany in the latter part of October.

United States.—Widespread occurrence of influenza began in September in the United States. In most communities, the epidemics affected persons of high school age first, then elementary school pupils, and lastly the adult population. Incidence appeared to be highest in the age group 5 to 19 years and least in the group 65 years of age and over. However, preliminary reports on deaths show that mortality was highest in the latter group. The epidemic appeared to reach its peak by mid-October and probably affected no less than 20 million persons throughout the country.

October

European and North American Asian strain influenza epidemics reached their peaks during October. Canada, the United States, and all but a few of the countries of Europe were experiencing declining epidemics as the month drew to a close. Peaks were passed early in October in Greece, Germany, Portugal, the Netherlands, Belgium, and England and toward the end of the month in the USSR, Switzerland, France, Austria, Ireland, and Spain. The northernmost countries of Europe—Finland, Sweden, Denmark, and Norway—were the last to be affected, as a group. The main force of the epidemics in these countries was not felt until early November.

In the Caribbean, Martinique, Jamaica, Cuba, Haiti, and Aruba reported epidemics during the month, while that in Puerto Rico subsided slowly. Most South and Central American countries were free of epidemic influenza by this time. Paraguay, reporting outbreaks early in October, was an exception. This relatively isolated country apparently experienced no epidemic during July and August when its neighbors were heavily affected.

On Oct. 22 an outbreak of influenza-like illness was reported among personnel at McMurdo Sound in Antarctica. Asian strain virus has not been identified from cases in the Antarctic, but if, as seems likely, the new strain was responsible for this outbreak, it can be said to have produced disease on every continent. The illness appeared at McMurdo soon after the arrival of spring supply ships bearing new personnel.

The eastern and southern regions of Africa were free of epidemic influenza by the first week of October. In the west, however, Ghana, which first noted influenza in mid-September, still reported active disease at the end of October. Certain portions of French West Africa experienced declining epidemics during the month, and a major new area of involvement was the Belgian Congo which reported an epidemic peak in early November. On Oct. 3 Algeria recorded its first Asian strain isolations, and as the month passed an epidemic in Morocco increased in intensity. Except for the Belgian Congo the interior of Africa remained apparently unaffected.

Only Japan, among Asiatic countries, experienced any major outbreaks or epidemics of Asian strain influenza in October. A sizable epidemic, carrying with it prominent excess mortality, visited Japan during the month. No other country reported such a second epidemic situation although several, including West Pakistan, Lebanon, Ecuador, and possibly Communist China, described minor outbreaks in communities which had experienced epidemics three to seven months earlier.

England.—After a summer of sporadic confirmed cases and outbreaks (as in the United States), influenza became widespread in England about Sept.

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18. Mortality statistics [*] indicate that a peak was reached between Oct. 5 and 19. Influenza deaths were predominantly in those over 55 years of age. The comparison of pneumonia and influenza mortality figures with those for previous years is striking (table 2).

Aruba.—The island Aruba, off the northern coast of South America, with a population of 56,000, received a supply of Asian strain influenza vaccine from the Netherlands in time to permit vaccination of a considerable number of professional persons, workers, and school children before an epidemic occurred. The epidemic, which peaked in late October, was mild with a low clinical attack rate. The impression on the island was that the vaccine had been of value in minimizing the epidemic. Nearby Venezuela and other Caribbean islands, such as Puerto Rico, Jamaica, and Martinique, apparently experienced much more severe epidemics.

USSR.—Asian strain isolates were obtained in Moscow as early as May, and sporadic isolations were made throughout the summer months, but influenza did not reach epidemic proportions in the country until October. The Asian strain was epidemic in Moscow in mid-October. Many schools and entertainment places were closed. While a vaccine was available (as in several other European countries including Sweden, Switzerland, the Netherlands, Germany, Denmark, England, and Italy), it was in short supply. In other parts of the country, at about the same time, influenza broke out, primarily in urban areas and along the principal lines of communication. Siberia was reported to be affected at the end of the month.

Japan.—An epidemic of apparently sizable proportions swept through Japan in the spring. This first epidemic, confirmed as due to Asian strain, reportedly peaked in mid-June and ended in mid-July. Influenza disappeared in August, only to reappear in epidemic form in late September and October. Again Asian strain isolates were obtained from numerous cases. Hundreds of schools were closed and excess mortality built up markedly in October. It is not yet clear whether this second Asian strain epidemic was the second phase of a split epidemic or if it represented a true reinfection epidemic. Preliminary studies suggest that reinfections may be relatively rare.[*]

November

Before the middle of November the Belgian Congo and the countries of Scandinavia had passed their epidemic peaks. No new major epidemics were in progress in any part of the world. Except in Japan, where the second Asian strain epidemic was subsiding, Asia remained apparently free of recurrent epidemics during November. North American, European, and northern South American countries consistently reported epidemic declines as the month progressed, and by the first week of December it seemed probable that the pandemic had run its course.

Almost every country had experienced epidemic Asian strain influenza by the middle of November. Only a few isolated islands and remote regions had not reported outbreaks. The central-interior area of Africa was apparently the largest of these unaffected regions. Difficulties in reporting rather than nonoccurrence of the new strain undoubtedly underlie many of the gaps in the present record.

TABLE 2.—*Aggregate Totals from Week Ending Aug. 24 Through Week Ending Nov. 23 for 160 Great Towns of England and Wales for 1953 through 1957*

Year	Pneumonia Deaths, No.	Influenza Deaths, No.	Total
1953	2,256	94	2,350
1954	2,302	119	2,421
1955	2,532	100	2,632
1956	2,510	95	2,605
1957	4,898	3,079	7,977

Comment

Pandemic Asian strain influenza had affected every continent, probably including Antarctica, by December, 1957. Major epidemics occurred in the majority of countries in each of these regions. Season was one of the more important determinants of the changing distribution of epidemics in those regions where seasonal changes are conspicuous. It is clear that the southern hemispheric countries where seasonal changes are marked, including those of southern South America, southern Africa, and Australia, were affected during their fall and winter. It is equally clear that Europe, the USSR, and North America were affected in the fall season of the Northern Hemisphere.

The timing of epidemics in many countries of the equatorial belt, however, must have been determined by other factors. Conditions for the occurrence of epidemic influenza are nearly constant throughout the year in the equatorial regions. The equatorial peoples, in general, have a constant year-round mode of life, while the peoples of regions where marked seasonal variations occur are more likely to vary their living habits considerably from season to season. Epidemics developed rapidly whenever the new virus was introduced into one of the many highly susceptible equatorial population groups, while introductions into similarly susceptible populations in Europe, North America, or southern South America (it is clear that such introductions were frequent in 1957) did not result in epidemics except at a specific time of the year—the fall-winter season.

It would seem that the most important timing factor for epidemic occurrence in the equatorial regions was the presence or absence of the virus in sporadic cases. Transportation facilities must therefore have been of great importance in determining the timing of epidemics in these areas. In regions

where seasons are well marked the situation was much more complex. Sporadic presence of the virus in a population was not enough to precipitate an epidemic. Seasonal living patterns and climate, which may not necessarily correlate with season—e. g., the United States, where fall in New England may be cold and windy while fall in the Southwest may be warm and mild—may have played roles in precipitating epidemics in those countries with well-defined seasons. In the regions far from the equator, greater crowding and more opportunities for close contact are more likely to exist in fall and winter. Varying conditions of crowding, times of school openings, and perhaps even the proportions of hours of darkness and light may also have been factors affecting the appearance of influenza epidemics.

While conditions of crowding and poverty often resulted in high attack rates, the ultimate distribution of pandemic influenza was not affected by crowding, although the timing of the epidemic in a particular region may have been. Many isolated areas of low population density were affected later than the nearest heavily populated areas. Crowded urban areas generally experienced epidemic peaks before rural regions within the same country.

Epidemic influenza spread world-wide in little more than six months, but there is evidence that dissemination of the virus throughout the world occurred within three to four months after the appearance of the new strain in Hong Kong. In the 1889-1890 pandemic world-wide spread required about 11 months. In the 1918-1919 pandemic spread was more rapid than in 1889, but world-wide involvement required several more months than in 1957. The apparent shortening of time necessary for world-wide spread in the most recent pandemic reflects the speed and extent of modern travel.

Summary

The new Asian variant of type A influenza made its first appearance in China in late February, 1957. During April, May, and June epidemic influenza spread throughout eastern Asia and the Middle East. During July and August many countries of South America and Africa were affected by the disease, and evidence was obtained of dissemination of the virus in Europe and North America. In September and October epidemic peaks were reached in many European and North American countries. By this time, most of Asia was free of epidemic influenza. November was a month of epidemic decline, and, by early December, the new strain had essentially completed its world-wide sweep. The spread of the disease was influenced by season in those regions where, because of their latitude, seasonal change is conspicuous. Thus epidemics occurred in the southern areas of the southern hemisphere between April and August and in the corresponding areas of the northern hemisphere between September and November. The equatorial regions, where seasonal change is less prominent, appeared to be affected as soon as the virus was introduced, regardless of the time of year.

Crowding and poverty were important determinants of attack rates in many countries. No differences in individual racial susceptibility were noted in 1957, although attack rates in some countries were higher in one cultural or racial group than in another. Social and economic differences among these groups often provided an explanation for the differing attack rates. The disease was clinically mild; attack rates were consistently high, particularly among children of school age. In crowded closed population groups, attack rates often reached or exceeded 70%. While the disease was generally mild, certain special risk groups, such as older persons, caused excess mortality to be affected strikingly in epidemic regions. Mortality was negligible, however, compared to that of the 1918 pandemic. The new Asian strain has produced the second influenza pandemic of this century and the first in the period of virological research.

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CARCINOMA OF THE LUNG

PRACTICAL CLASSIFICATION FOR EARLY DIAGNOSIS AND SURGICAL TREATMENT

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Among 489 patients with the diagnosis of bronchogenic carcinoma, there were 291 in whom surgical exploration was carried out. The carcinoma was found in a main bronchus in 71 (24%), in a lobar bronchus in 156 (54%), in a mid-lung zone in 31 (11%), and in a subpleural location in 33 (11%). The highest rate of resectability (94%) was among the 31 mid-lung carcinomas, while the subpleural group were the least favorable. The greatest rewards in resectability were thus found in the group of patients in whom bronchoscopy is always negative, the diagnosis being made by following up the suspicious shadow seen on the chest roentgenogram by exploratory thoracotomy. Operative mortalities were about the same in the four groups, but early postoperative results were best in the group with mid-lung cancer (86% of those surviving surgery being alive after one year). The "negative" chest film from previous examinations, when compared to the x-ray under consideration, supplies the key information in making an early diagnosis of lung cancer. Therefore, this film should be considered as one of the patient's most valuable possessions. If storage facilities in an x-ray department are limited, such films should be given to each patient to keep for himself.

The incidence of primary carcinoma of the lung is increasing at an alarming rate, for it not only has become the most common visceral carcinoma in males but has passed pulmonary tuberculosis as a cause of death.[1] Until some specific form of cure is found that will destroy or negate the cancer cell wherever it is located in the body, our efforts must be directed toward improving results with present-day methods. When bronchogenic carcinoma is confined to the lung, it is curable by pulmonary resection. It follows, therefore, that the detection of this cancer in greater numbers before it has spread beyond the lung will make it possible to improve the surgical cure rate.

Since the original successful pneumonectomy for bronchogenic carcinoma, in 1933, by Graham,[2] emphasis has been placed upon bronchoscopy as the most important means of detecting this neoplasm. It is reported [3] that as high as 65% of the cases may be diagnosed by bronchoscopy. However, with the realization that carcinoma may arise anywhere in the lung, even in the peripheral portions, it is obvious that there is a wide range of cases that are outside the limits of bronchoscopic visibility and biopsy. In only about one-fourth of the cases herein reviewed was it possible to obtain a positive biopsy at bronchoscopy. Furthermore, in our experience, the smears of the sputum stained for cancer cells have been helpful in making a certain diagnosis of carcinoma in only a small percentage of the cases. Therefore, proper evaluation not only of the signs and symptoms but of the x-ray findings must remain as an important factor in the early detection of this neoplasm.

To facilitate an understanding of early diagnosis, we have divided our cases of bronchogenic carcinoma into four main categories: (1) main bronchus, (2) lobar bronchus, (3) mid-lung, and (4) subpleural. Of the 489 cases, 198 were considered nonexplorable, according to standards presented later, and in 291 instances surgical exploration was carried out. Since in the advanced cases the spread of the cancer to both the mediastinum and pleura makes the site of origin of the carcinoma difficult to determine, the statistical results of our study are confined to the 291 cases in which a thoracotomy was performed.

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Carcinoma of the Main Bronchus

In 71, or 24%, of the 291 operated patients, cancer was found to arise in the main bronchus or tissue immediately adjacent to the bronchus so as to invade the walls (fig. 1). The early symptoms are those of bronchial irritation and then obstruction. This type of carcinoma is difficult to detect by x-ray early in its development because the main bronchi are covered by the heart and great vessels and, therefore, do not present a shadow detectable

on the chest roentgenogram. However, the bronchoscopy will invariably reveal the presence of this tumor which can be confirmed by biopsy or smear of the lesion. The duration of symptoms was from one month to one and one-half years, and in one case the patient was asymptomatic. The main symptom was that of cough which was dry at first and then was productive of sputum. In the case of

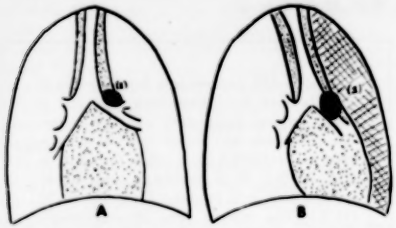

Fig. 1.—Carcinoma of the main bronchus (bronchoscopy positive). *A*, early stage in which x-ray may or may not show mass (1) at hilus. *B*, late stage.

cigarette smokers, who made up about 90% of this series, it was sometimes difficult for the patient to determine exactly when his cough had become more severe. Hemoptysis and wheezing were the most important additional symptoms and were present in three-fourths of the cases in which resection was carried out. These cardinal symptoms of main bronchus carcinoma are urgent indications for bronchoscopy. The presence of this serious malignancy may be detected by this technique long before a significant shadow is seen on the chest roentgenogram or constitutional symptoms are present.

However, when the obstruction of the bronchus becomes more advanced, bronchial drainage is impaired, and secondary changes in the lung are noted. In our series these changes included recurrent and persistent pneumonitis, lung abscess, and lobar to total atelectasis (fig. 1). Most often, when the main bronchus is totally occluded, the carcinoma has spread to the hilus to invade the pulmonary artery and anterior vein which lie in close proximity to the main bronchi. This proved to be the chief cause of nonresectability in those cases of main bronchus carcinoma which were explored. With intrapericardial ligation of the vessels, which was carried out in over half of the resected cases, the resectability rate may be increased.

Carcinoma of the Lobar Bronchus

Carcinoma arose in the primary or segmental orifices of the lobar bronchus in 156, or 53%, of the patients in the series studied. Bronchoscopy revealed the lesion in one-third of this group (fig. 2), although collateral information, such as bronchial compression and distortion, was gained in an additional one-fifth of the cases. Eight of the patients in this group were entirely asymptomatic and showed only an x-ray lesion as the main evidence of bronchogenic carcinoma. In the remainder of the series, the symptoms of cough, hemoptysis, and wheezing, together with those of acute respiratory infection, were most prominent. In fact, the common initial events in this group were the symptoms and signs of an acute bronchopulmonary infection.

One cannot emphasize too much the adverse effect that the use of antibiotics has had on the masking of symptoms of bronchogenic carcinoma in this particular group of patients. Bronchopulmonary infection is a common sequela of bronchial obstruction from carcinoma. In the preantibiotic era, infection persisted so that both the patient and physician were alerted to the possibility that there was some other condition responsible for the persistence of this infection. However, with the present-day widespread use of powerful antibiotics, the infection is controlled in spite of bronchial obstruction, and both the patient and the physician are lulled into a sense of false security with the control of this infection.

Many patients are treated without any x-ray record of the disease. Certainly any patient who has had a severe respiratory infection severe enough to warrant antibiotic therapy should have a chest roentgenogram, preferably at the beginning of the treatment but certainly following it. For the persistence of an x-ray shadow following the subsidence of an acute symptomatology of infection should lead to investigation for possible carcinoma.

Failure of a lung abscess to resolve completely following appropriate antibiotic therapy and bronchial drainage should be considered as evidence of probable pulmonary malignancy. Similarly, the

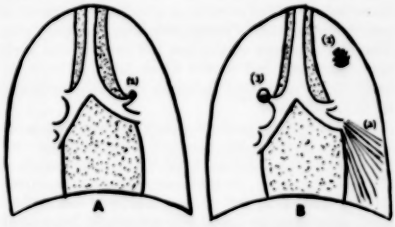

Fig. 2.—Carcinoma of lobar bronchus (bronchoscopy may be positive). *A*, early stage showing perihilar mass (1) as indicated by x-ray. *B*, late stage showing (1) pneumonitis, (2) atelectasis, and (3) abscess.

clinician must regard the discovery of a pulmonary cyst in a person in the cancer-age group as a sign of carcinoma until proved otherwise. Previous films are particularly helpful in these cases. Atelectasis and pneumonitis secondary to carcinoma, if treated

with repeated courses of antibiotic therapy, may be present for a long period of time without causing serious symptomatology. Failure to discover a lobar carcinoma on bronchoscopy in no way rules out the presence of this malignancy, for in two-thirds of the cases in this series the malignancy arose beyond the limits of bronchoscopic visibility and was proved only by exploratory thoracotomy.

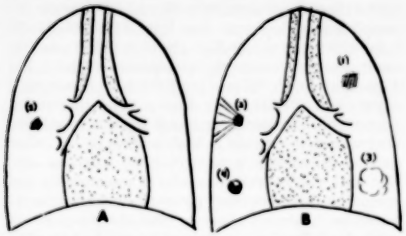

Fig. 3.—Carcinoma of midlung (bronchoscopy negative). *A*, early stage showing x-ray shadow at (1). *B*, late stage showing (1) localized persistent pneumonitis, (2) localized atelectasis, (3) localized emphysema, and (4) rarefaction in solid shadow.

Carcinoma of the Mid-lung

In this series of patients there were 31 in whom the carcinoma arose in the mid-lung zone, free from the hilus or pleura (fig. 3). In no instance was the tumor visible by bronchoscopy, and in only four cases was the collateral information obtained at bronchoscopy evidence of spread of the tumor to the mediastinal lymph nodes. In eight of these patients no symptoms were present, and only a persistent shadow in the lung field was the main finding pointing to bronchogenic carcinoma. Many attempts have been made to lay down absolute diagnostic criteria to distinguish the benign from the malignant mid-lung lesion. Although the irregularity of the border and dimpling may be noted, these findings are not infallible guides.

Skin tests and serologic tests for the common granulomas are most helpful in the group below 40 years of age, but they rarely affect the decision for exploratory thoracotomy in patients above the age of 40. In a like manner, scalene node biopsy and sputum studies for cancer cells have been positive seldom in our experience in the mid-lung cancer group except in the obviously advanced cases. Similar findings have been reported in the medical literature where careful studies of mid-lung carcinoma have been recorded.[4]

Of course, metastatic malignancy to the lung may simulate bronchogenic carcinoma, and a careful history and physical examination may point to the extrapulmonary possibility which will be proved by special studies. However, in the absence of localizing signs or symptoms, a complete radiologic inventory of each organ and system is rarely indicated. Metastatic malignancy to the lung is usually multiple, and planograms of the lung are most helpful in demonstrating minute metastases invisible on conventional films. In the symptomatic group of patients with mid-lung carcinoma, the most prominent symptoms were those of mild pulmonary infection which responded to antibiotic treatment and yet showed the persistent pulmonary shadow as the main clinical feature. Calcium deposits were present in two instances in the lesion, and, as has been shown by others,[4a] their presence does not rule out the presence of a bronchogenic carcinoma.

A review of these cases reaffirms the conviction of the physicians who have had extensive experience with this problem, that the so-called solitary lesion or coin lesion (the smaller and more circumscribed variety) is best treated by surgical excision.[4] Reported series of cases have shown definitely that the percentage of cases of bronchogenic carcinoma that are found reflects to a major extent the age group of the patients who have these lesions removed. Thus, in those series where the majority of the patients are below the age of 40 years, there is a lowered percentage of carcinoma, around 11%,[4b] while in series of patients in which the older age group predominate, as high as 50% may show bronchogenic carcinoma.[4c] Our experience with these solitary circumscribed pulmonary lesions adds conclusive evidence that excision is the treatment of choice.

Subpleural Carcinoma

In this series there were 33 instances of carcinoma arising in the lung immediately beneath the visceral pleura (fig. 4). In no one of these patients was the tumor visible by bronchoscopy, although collateral inflammation due to spread to hilar lymph nodes, producing partial bronchial obstruction, was present in seven instances. These patients presented the clinical syndrome greatly

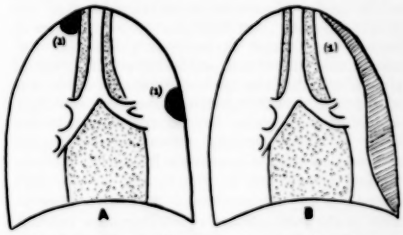

Fig. 4.—Carcinoma of subpleural region (bronchoscopy negative). *A*, early stage showing (1) mass indicated by x-ray and (2) apical (Pancoast) tumor. *B*, late stage (inoperable) indicating massive bloody pleural effusion at (1).

different from those in the three other groups that we have just considered. Pleural pain which was generally interpreted as being an acute pleurisy that persisted to the chronic state was the main symptom. Later on, intercostal pain signaled the involvement of the intercostal nerves. Cough was a late symptom. Hemoptysis occurred in only 4 of the 33 patients as a sign of advanced carcinoma. X-ray reveals a small subpleural shadow early in the disease (fig. 4). Most often, pleural fluid which developed as the result of direct invasion of the pleura was serous at first and then characteristically had a bloody appearance. The presence of extensive involvement of the pleura was considered as evidence of inoperability. When the apex of the pleural cavity was involved, the syndrome of the so-called Pancoast tumor was present. This was characterized by pain involving the shoulder and arm, signs and symptoms of brachial plexus involvement, and Horner's syndrome. Such patients are rarely amenable to surgery.

Criteria for Operability

In each instance in the group of 198 patients in whom no thoracotomy was performed, careful consideration was given to the possibility of an exploratory operation. To our knowledge, no patient was refused surgery in whom we thought there was a chance for successful surgical excision of the lung cancer. In most instances, a combination of factors was present in any one given case. Primarily, the patient was studied from the point of view of whether the cardiopulmonary reserve was adequate to permit successful pulmonary resection. Spread of the cancer beyond the thorax to the brain, abdomen, osseous system, cervical region, etc., was considered a contraindication to surgery. Marked weight loss is often a sign of extensive metastases of the carcinoma. Extensive involvement of the mediastinum as evidenced by vascular obstruction, chronic or recurrent laryngeal paralysis, or Horner's syndrome was the second group of signs and symptoms used as a deterent to surgery. Finally, involvement of the pleura and chest wall as shown by massive effusion and identification of cancer cells in the fluid were considered contraindications. Most of the patients had a combination of the above factors mentioned. In a few instances surgery was advised but was refused by the patient.

TABLE 1.—*Resections Performed in Patients Subjected to Exploratory Thoracotomy*

Region	Total Cases, No.	Pneumonectomy	Lobectomy	Nonresectable	% Resected
Main bronchus	71	51	0	20	69
Lobar bronchus	156	70	25	61	61
Mid-lung	31	21	8	2	94
Subpleural	33	5	9	19	42
Total	291	147	42	102	65

Resectability

In those patients subjected to exploratory thoracotomy, the number of resections in each group is shown in table 1. The striking figure is that observed for the mid-lung carcinomas in which 94% of the neoplasms were resectable. The neoplasms of the main bronchus and lobar bronchus were the next most favorable groups for resection, showing about the same resectability (69 and 61%), while the subpleural group was the least favorable, with only 42% being resectable. The number of cases in each category, with the exception of the lobar bronchus group, is too small to be of statistical significance. Yet they do show a trend that is important, for the mid-lung group has a resectability that was almost twice as high as that of the other groups. This figure is important, for it stresses the fact that the greatest rewards in resectability are found in this group of patients in whom bronchoscopy is always negative, and the diagnosis is made by following up the suspicious shadow seen on the chest roentgenogram by exploratory thoracotomy.

Operative Mortality

The operative mortality for the various groups of patients did not vary a great deal. There was an average of 9.6% operative deaths for the entire group. The individual operative mortalities of the various groups are as follows: main bronchus, 9%; lobar bronchus, 10%; and mid-lung and subpleural, approximately 6% each. Although some changes were made in the surgical technique during the treatment of these patients, it varied little, for the surgery was performed by one of us (L. A. B.). There is no significant difference in the causes of death in the various groups studied. Cardiac and pulmonary failure and pneumonitis and embolic phenomena were the major causes. Thus, the risk of surgery seems to resolve itself to the inherent risk of pneumonectomy and lobectomy in persons in the older age group. If more lobectomies can be done, then the mortality will be lessened. If the operator confines his surgical explorations to only the best risk group, a lower mortality can be achieved also. However, there is no question that a number of possibly curable patients will be denied the chance to have the cancer removed.

Results

The majority of the patients who have been operated on in this group have been treated in the past five years, so longtime follow-up results are not available. The early results in the group with mid-lung cancer are the best, for only five patients (16%) died in the first year after surgery; the rest lived from one to nine years following operation. In the group with cancer of the main bronchus, 18% died during the first year, while 21% of the group with lobar cancer died. The poorest survival

rate during the first year was in the group with subpleural cancer, where 42% died during this period of time. Although there is very little difference in the survival rate in the first three groups, the subpleural group, apparently due to early invasion of the pleural lymphatics, has a poor chance for long survival.

Many factors enter into survival. The types of carcinoma found in our patients are listed in table 2. There was a high percentage of anaplastic carcinoma (54%) in the subpleural group, whereas in the other categories the percentage of anaplastic carcinoma varied from 22 to 28%. The duration of symptoms was one to three years in all groups except in the mid-lung group where asymptomatic cases were present in the highest proportion and where those with symptoms had had them only from one month to one and one-half years. No significant age difference was noted. Fewer lymph node metastases were seen in the mid-lung group. Blood vessel invasion by the carcinoma, reported by Collier and others,[5] and its importance in survival time, are being studied. Furthermore, since all carcinoma is asymptomatic at onset, the real duration of the disease cannot be estimated. Overholt [6] has recently concluded, in studying his five-year survivals, that it is the prompt recognition and excision of the carcinoma that in the last analysis is the most important thing. Our studies of the early survivals are in accord with this conclusion.

Comment

In presenting the various types in this classification of bronchogenic carcinoma, we have stressed the importance of the x-ray finding as the means of pointing the way to exploratory thoracotomy. Obviously, since the diagnosis is made mainly at thoracotomy, nonmalignant lesions will be removed. One can reasonably ask: What are these nonmalignant lesions, and is surgical excision of them indicated? A study of nonmalignant lesions simulating bronchogenic carcinoma has been reported by one of us (L. A. B.).[7] Two-thirds of the lesions proved to be inflammatory on surgical excision, while one-fifth were benign tumors, and the remainder were developmental defects. In 77% of the patients cure could not be expected by conservative means. Twenty per cent fell into the borderline group and 3% were probably not benefited by surgery.

Our present larger experience with this group of conditions simulating bronchogenic carcinoma, and that of many others in the medical literature, supports the findings in the earlier reported series. Thus, if the patients with benign lesions simulating bronchogenic carcinoma are best treated in the vast majority of instances by surgical excision, there can be no valid argument against exploratory thoracotomy when the criteria for operability previously enumerated in this discussion have been fulfilled. On the other hand, exploratory thoracotomy is not warranted in debilitated patients with far-advanced disease in whom complete resection or even palliation is obviously impossible, for it may entail a definite morbidity and mortality. This often poses a difficult clinical decision, for palliative x-ray or nitrogen mustard therapy should not be administered without a positive cellular diagnosis for carcinoma. Needle biopsy through the chest wall in the obviously nonresectable case is occasionally helpful for peripheral lesions, although its routine use is dangerous and unwarranted. Repeated sputum studies for cancer cells and scalene biopsies are indicated. Although we have been disappointed with our results in obtaining positive Papanicolaou stains of the sputum for cancer cells in the operable cases, the number of positives in advanced cases have made this test worthwhile.

Recognition that the chest roentgenogram is an integral part of a complete physical examination, the use of preemployment films, and mass survey studies have increased the number of asymptomatic lesions of the lung that have been clinically detectable. More and more people are having an annual chest x-ray examination. Thus, the films reported as showing no pathology form an important base line upon which subsequent abnormality in the roentgenogram may be judged. It has been the good fortune for some of our patients to have available such films. In figure 5, *left*, a circumscribed shadow of the lung is seen on a routine chest film. This could be diagnosed as a new asymptomatic lesion only by the comparison with the negative film taken a year before. Thus there was an urgent indication for surgical exploration, which made possible the excision of a bronchogenic carcinoma. The patient has been perfectly well for almost a decade and shows no evidence of recurrence on an x-ray taken over nine years after operation (fig. 5, *right*).

TABLE 2.—*Types of Carcinoma Found in Patients Subjected to Exploratory Thoracotomy*

Region	Cases, No.	Type		
		Anaplastic Cell	Adenocarcinoma	Squamous Cell
Main bronchus	71	20	10	41
Lobar bronchus	156	46	44	66
Mid-lung	31	7	11	13
Subpleural	33	18	11	4
Total	291	91	76	124

The importance of saving the "negative" chest film has not been stressed in the medical literature. For it is still a common policy with many x-ray departments in hospitals, private clinics, and offices to dispose of the film after a period of from three to five years. Recently, microfilming has been introduced as a means of conserving storage space; however, the use of this modality is far from universal. This study offers convincing proof of the

great value to the patient of having the previous actual film available for comparison. It may offer the deciding evidence that this asymptomatic lesion is possibly a bronchogenic carcinoma, and by excision of the carcinoma the life of the patient may be saved. Thus, the previous film may be one of the patient's most valuable possessions. It may be just as lifesaving to him as a safety belt in his car or life preserver in his boat. If facilities are not available for the preservation of films in an x-ray department after five years, then these films should be given to each patient to keep for himself.

There was no significant difference in operative mortality of the various groups. The survival following operation during the first year was approximately 82% for the first three groups but only 52% for the patients with subpleural cancer. The most important single factor in the decision for exploratory thoracotomy in those patients in whom the bronchoscopy was negative was the proper interpretation of the chest roentgenogram which takes into consideration the patient's signs and symptoms. Preservation of the chest film is of vital importance to the patient. By comparing this film with subsequent ones, slight changes indicative of early bronchogenic carcinoma may be detected. Greater effort must be made by all physicians who take chest roentgenograms to see that all of these films are preserved, microfilmed, or given to the patient.

Fig. 5.—*Left*, small asymptomatic lesion, left midlung field, removed as carcinoma because it was not seen on annual film taken one year previously. *Right*, x-ray of same patient, apparently cured, nine years after removal of carcinoma. One mediastinal lymph node, positive for carcinoma, was removed in this patient. Opaque left lung field is typical of organized postpneumonectomy pleural space. Patient is now performing full-time office work.

Summary

A practical classification of bronchogenic carcinoma into (1) main bronchus, (2) lobar bronchus, (3) mid-lung, and (4) subpleural carcinoma has been based upon a study of 489 patients, of whom 291 were subjected to thoracotomy. Main bronchus cancer occurred in 24% of the operated patients. Bronchoscopy was invariably positive and resection was carried out in 69% of the patients in whom an exploration was done. Lobar bronchus carcinoma was seen in 54% of the operated group. Bronchoscopy revealed the tumor in about one-third of the cases and there was a resectability of 61%. Mid-lung cancer was present in 11% of the operated cases. Bronchoscopy failed to show the tumor. In 94% of the operated cases resection was possible. Subpleural carcinoma occurred in 11% of the patients in the operated group and was beyond the limits of bronchoscopic visibility. Only 42% of the operated cases were resectable.

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SELECTIVE SEGMENTAL BRONCHOGRAPHY

André Mackay, M.D., Armand Trépanier, M.D.
and
Maurice R. Dufresne, M.D., Montreal, Canada

The technique of bronchography here described has been used in 335 cases and has frequently demonstrated the exact nature of pulmonary lesions. Local pharyngeal anesthesia permits the insertion of a selected Metras catheter of appropriate shape and size whereby radiopaque substance can be placed selectively in parts of the lung, including the apical segment of each upper lobe, that were formerly inaccessible. The catheters are inserted during fluoroscopy; they are guided by the endoscopist while their position is verified by the radiologist. Abnormal images are observed and recorded instantly on spot films. The contrast medium used, aqueous Dionosil, was found to have several advantages; it seldom filled the alveoli and it disappeared rapidly from the bronchi. Complete bronchograms so obtained were valuable to the surgeon in delimiting his field while making sure of the complete excision of all diseased segments.

The purpose of this paper is to present a method of bronchography which provides visualization of each bronchial segment and demonstrates the presence and, frequently, the exact nature of a pathological lesion.

Anesthesia

Thorough local anesthesia is achieved with use of pharyngeal sprays of a 2% solution of tetracaine (Pontocaine) hydrochloride or a 4% solution of cocaine and intratracheal instillations of a 2% concentration of lidocaine hydrochloride with epinephrine. Premedication consists of (1) 0.1 Gm. (1½ grains) of secobarbital given one hour before the beginning of anesthesia, (2) 0.4 mg. (1/150 grains) of atropine sulfate when indicated, and (3) 60 mg. of alphaprodine (Prisilidene) hydrochloride at the beginning of anesthetization. The last-mentioned drug has many advantages over morphine in that it does not produce nausea and its action is rapid (three to five minutes if injected hypodermically or 30-60 seconds if intravenously). The short duration of its effects (approximately two hours) is useful in treatment of nonhospitalized patients. In addition, its dosage is adjustable to the needs of the patient.

Catheters

Since 1954, we have been using catheters designed in 1947 by Henri Metras.[1]

These catheters, shown in figure 1, include the following: (1) a small, curved catheter for selectively making opaque the basal segments of the lower lobes; (2) a medium-sized curved catheter for use in the middle lobe, the dorsal segment of the lower lobes, or the upper lobes as a whole, used for routine bronchograms; (3) a large, curved catheter for use in the apical segment of the upper lobes; and (4) two double curved catheters, the curves being in a different plane; one is used in the anterior segment of the right upper lobe or the posterior segment of the left upper lobe, and the other in the posterior segment of the right upper lobe or the lingula.

From the Chest Clinic, Notre-Dame Hospital.

Based on a paper read before the Section on Radiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

It was often impossible with the earlier catheters to reach the apical segment of each upper lobe, the lingula, and the anterior or posterior segments of the upper lobe; these can now be made opaque at will. This fact is even more striking when broncial distortion, tumor, or a ventilation defect is present. In normal lungs, inspiratory suction easily produces opacity of all the bronchopulmonary segments, regardless of the technique employed.

Technique

The appropriate Metras catheter is introduced with use of mirror vision (or vision through the bronchoscope) and later is guided with fluoroscopic control into the appropriate lung, lobe, and segment.

After the diseased segment has been made opaque (fig. 2), the bronchogram is completed with use of the same catheter. In certain favorable cases, a bilateral bronchogram is done, which seldom requires more than a total of 20 cc. of the radiopaque substance for both lungs.

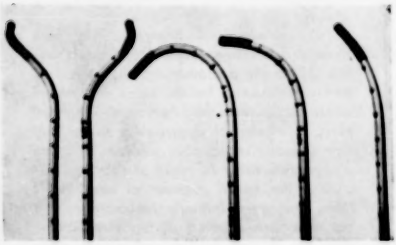

Fig. 1.—Metras catheters which permit any segment of either lung to be reached at will.

Dionosil

Since August, 1952, we have performed 335 bronchograms with aqueous Dionosil (propyl ester of 3, 5 diiodo-4-pyridone-*N*-acetic acid in water suspension with carboxymethylcellulose added). It usually stops showing up on the chest films within 48 hours.[2] We have observed no untoward reaction due this medium except a slight rise of temperature (1 F) the following day in about 5% of the cases.[3]

Radiology

It must be emphasized that a close cooperation between the endoscopist and the radiologist is essential for making a satisfactory bronchogram. During fluoroscopy, the endoscopist guides the Metras catheter, with its position checked by the radiologist, into the desired segment. The radiologist judges the amount of dye to be injected to obtain double contrast pictures (fig. 3). This is easily done with Dionosil, which adheres readily to the bronchial mucosa. If there is an important narrowing or complete stenosis, the bronchus is filled completely to assure that nonopacity is not due to a faulty technique. Sometimes no dye passes the stenosis (fig. 4), but the catheter can be pushed through and thus both sides of the lesion can be visualized.

Lateral and oblique spot films show more precise anatomic landmarks than the posteroanterior view. Except in obese patients, these are taken without the fixed grid and the exposure time can be lowered to one-thirtieth of a second.

Before withdrawing the catheter, the radiologist must see that for all segments of a lung injections have been made and recordings done, especially in patients with bronchiectasis. Then, standard posteroanterior, lateral, and oblique films are made. This technique may be more time consuming than others, but we believe that it can improve the diagnostic accuracy of bronchography.

Incomplete bronchograms are due to insufficient bronchial filling or to technical defects of the films. The blind postural technique usually employed often results in partial filling, even when no important lesion is seen on the plain films. This can happen even more frequently if there exists a segmental or lobar lesion decreasing the ventilation of that portion of lung. There is also the possibility of the emptying of one or many segments between the time of injection of the opaque substance and the taking of the standard films.

With the technique just described, abnormal images are observed and recorded instantly on spot-films. Moreover, the presence of a lesion may be suspected on the standard 14-by-17-in. radiographic bronchograms and the true nature or exact localization of this lesion may be realized only on a spot film with the correct projection (fig. 5).

Fluoroscopy and spot films are just as important in the study of the bronchopulmonary tree as they are in the study of the gastrointestinal tract. A complete bronchogram on the first attempt will avoid tedious repetitions and may prevent unnecessary surgery in that the exact dissemination of the lesion is known; it will also permit complete excision of all the diseased segments. Dr. Overholt[3A] insisted on this aspect of the problem a few months ago, and we feel that a large responsibility in these cases rests with the radiologist-endoscopist team.

Nordenström[4] described in October, 1955, a new bronchographic technique with aqueous Dionosil. The patient is placed in the lateral position, and, with use of the fluoroscopic screen, 15-20 cc. of the opaque substance is injected rapidly into the main bronchus at the end of extreme expiration (fig. 6). The next inspiration coats the bronchi with a thin film of the opaque substance. The segments not injected are then filled selectively (fig. 7). However, we prefer to insert first the appropriate catheter into the segments in which pathology is suspected and then complete the bronchogram. Alveolar filling seldom occurs, even when the bronchi are flooded (fig. 8).

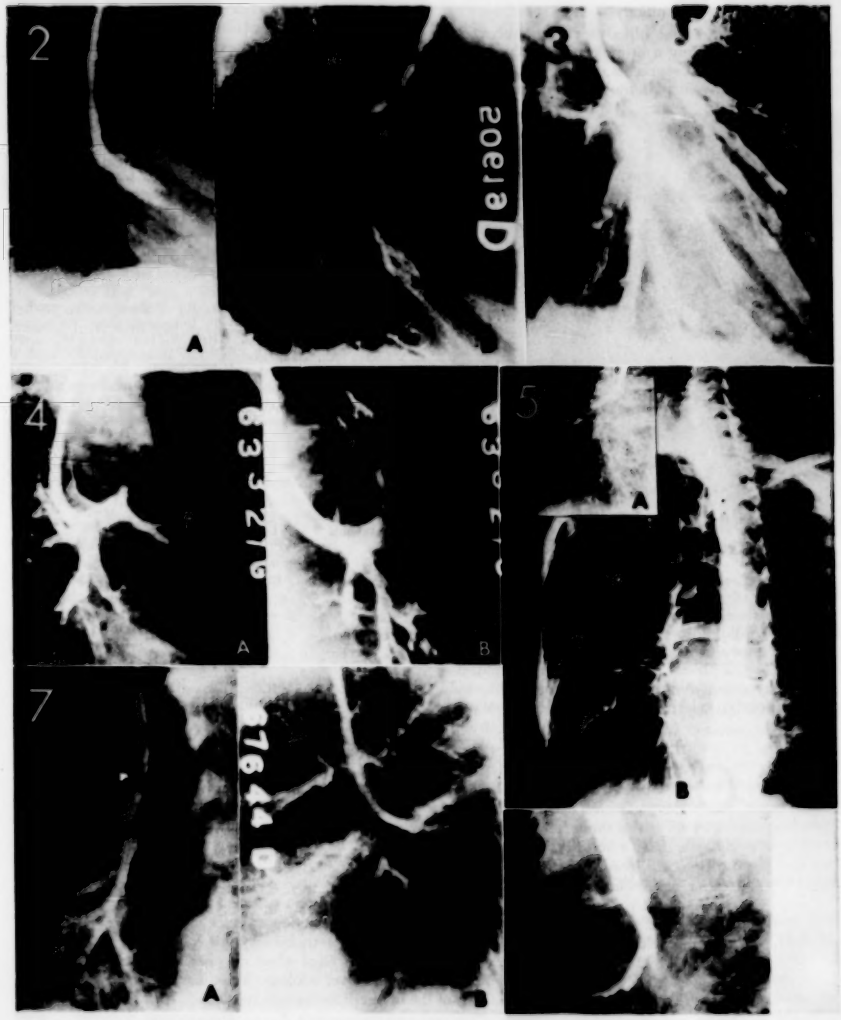

Fig. 2.—*A*, Diseased middle lobe, into which the proper catheter has been inserted. *B*, the same catheter is used to complete the bronchogram. Fig. 3.—Spot film of left lung in right anterior oblique view, showing fusiform bronchiectasis of lingula and all segments of lower lobe in double-contrast. Fig. 4.—*A*, stenosis of left upper lobe bronchus, beyond origin of lingula, which is narrowed. No dye has passed stenosis in spite of complete filling. *B*, catheter has been pushed through the narrowing, making apical-posterior segment opaque. Anterior segment was completely occupied by neoplastic mass. Fig. 5.—*A*, spot film in right posterior oblique view showing a cavity filled with Dionosil in anteromedial segment of middle lobe. *B*, standard film in left anterior oblique view few minutes later. Cavity has completely emptied and is no longer visible. Fig. 6.—Nordenström's technique. Fifteen cubic centimeters of Dionosil has been injected rapidly into right main bronchus at end of forceful expiration. Fig. 7.—Nordenström's technique. *A*, inspiratory suction has filled all the segments of the three lobes, except dorsal segment of the right lower lobe. *B*, this segment is then opacified selectively and film shows bronchiectasis.

Summary

Fluoroscopy and spot films are often necessary to visualize adequately a bronchopulmonary lesion and to assure that all segments of a lung have been injected, especially in patients with bronchiectasis.

Fig. 8.—Absence of alveolar filling, even though bronchi are flooded.

Special Metras catheters are useful in selectively reaching certain diseased segments. The cooperation of the radiologist and endoscopist is essential for a satisfactory bronchographic study.

In 335 cases, aqueous Dionosil (propyl ester of 3, 5 diiodo-4-pyridone-*N*-acetic acid in water suspension with carboxymethylcellulose added) proved to be the ideal bronchographic medium, at least for the time being, because it disappears rapidly from the bronchi, it produces double-contrast pictures, there is seldom alveolar filling, even when the bronchi are flooded, there is no known sensitivity to this substance, as it does not break down into inorganic iodine, it causes little or no granulomatous reaction in the lung, and the irritation it produces on the bronchial mucosa can be symptomatically controlled by adequate premedication and local anesthesia.

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CLINICAL MANIFESTATIONS OF HISTIOCYTOSIS X.—As a result of the case reports of histiocytosis X or normocholesteremic xanthomatosis published the past three decades, it has been possible to appreciate the protean manifestations of this group of diseases. It is now apparent that these manifestations encompass many clinical fields and that the disease may be encountered in various specialties. . . . Because of the manner in which they have evolved, the nosologic classification and nomenclature of this group of diseases have been confusing. The three syndromes of eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease, which were originally regarded as distinct entities, are now considered to be interrelated manifestations of a single malady. The term histiocytosis X has been suggested by Lichenstein to include these three diseases all of which are characterized pathologically by a histiocytic proliferation of unknown etiology. Thannhauser has used the terms "essential xanthomatosis of the normocholesteremic type" and "eosinophilic xanthomatous granuloma" as synonyms of histiocytosis X. . . . Histiocytosis X may now be considered along with tuberculosis, syphilis, neoplasia, lymphoma, sarcoidosis, and collagen disease as a disorder with protean manifestations. The organs or systems chiefly involved are bone, brain, lung, skin, reticuloendothelial system, and certain mucous membranes. The etiology of the group of diseases is unknown.—J. L. Dadey, M.D., and L. M. Hurxthal, M.D., Clinical Manifestations of Histiocytosis X in the Adult, *Journal of Chronic Diseases*, November, 1957.

SMOKING AND DEATH RATES—REPORT ON FORTY-FOUR MONTHS OF FOLLOW-UP OF 187,783 MEN

I. TOTAL MORTALITY

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and
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Total death rates in relation to smoking habits were studied in 187,783 men who were traced for an average of 44 months. Particular attention has been given to possible sources of bias in the data. Inclusion of each man in the series was determined on the basis of a questionnaire; death certificates were obtained on every one of the 11,870 men recorded as dead at the end of the 44-month period of this study. A total of 4,406 deaths occurred among men with a history of regular cigarette smoking only. This was an excess of 1,783 over the number that would have occurred had their age-specific death rate been the same as for men who never smoked. The mortality ratios were higher in the groups who smoked the largest number of packs per day, and cigarette smoking appeared to have far more effect on the death rate than did pipe or cigar smoking.

This report gives an analysis of death rates in relation to the smoking habits of 187,783 men who have been traced for an average of 44 months. The first results of the study were presented when the subjects had been traced for 20 months.[1] The major findings at that time were that (1) the death rate of cigarette smokers was far higher than the death rate of men who had never smoked cigarettes, and (2) deaths ascribed to cancer accounted for about one-quarter of the excess deaths among cigarette smokers, while deaths ascribed to coronary artery disease accounted for over one-half the excess.

The study was continued for another two years to check on the earlier findings and to obtain more detailed information on many points of interest, such as the effect of giving up smoking. The new information fully confirms the above findings.

Part 1 of this report is concerned with total death rates in relation to smoking and with analysis aimed at determining the reliability of the findings. Part 2 is concerned with death rates from specific diseases.

Procedures

After designing and pretesting a smoking questionnaire, we trained over 22,000 American Cancer Society volunteers as researchers for the study. Each researcher was asked to have the questionnaire filled out by about 10 white men between the ages of 50 and 69 whom she knew well and would be able to trace. The researchers were told not to enroll a man if he was seriously ill or if they knew he had lung cancer. Once a year thereafter, they reported on each man as "alive," "dead," or "don't know" and recorded all changes of address. A copy or abstract of the death certificate was obtained on each death reported. Whenever cancer was mentioned on a death certificate, further information was sought from the doctor, hospital, or tumor registry. The study area included 394 counties in nine states: California, Illinois, Iowa, Michigan, Minnesota, New Jersey, New York, Pennsylvania, and Wisconsin.

The enrollment of subjects began on Jan. 1, 1952, and continued until the summer of that year. A total of 204,547 smoking questionnaires were collected, but it was decided to exclude 6,288 men enrolled after May 31, 1952. An additional 8,396 questionnaires were excluded because of duplication, incompleteness of information, or administrative difficulty. Nine questionnaires, all showing a history of regular smoking, were sent to us with the notation that the men had cancer, seven being specified as lung cancer; these were also excluded. This left a net total of 189,854. About three-quarters of these subjects were enrolled between Feb. 9 and March 11, 1952, the mean date of enrollment being Feb. 27, 1952.

Follow-up procedures were started on Nov. 1 of each year from 1952 through 1955. As of Oct. 31, 1955, the volunteers had reported 175,913 (92.7%) of the men as alive, 11,870 (6.2%) dead, and 2,071 (1.1%) lost to follow-up. Thus, 187,783 were reported by the volunteers as traced. Those still alive as of Oct. 31, 1955, had been in the study for an average of 44 months. The total experience covered 667,753 man-years, a suitable adjustment being made for the years of life lost by those who died.

A copy or abstract of the death certificate was eventually obtained on every one of the 11,870 men recorded as dead. An additional 15 deaths

From the Statistical Research Section of the American Cancer Society.

A summary of this paper was read in the General Scientific Meetings at the 106th Annual Meeting of the American Medical Association, New York, June 4, 1957.

This is the first part of a two-part article to appear in consecutive issues of THE JOURNAL.

were reported by the volunteers, but, since we were unable to locate the death certificate or other official document to verify the fact, these were classified as lost to follow-up in the figures given above.

TABLE 1.—*Man-Years of Exposure to Risk by Type of Smoking (Lifetime History) and by Age at Start of Study*

Type of Smoking	Age Group, Yr. 50-54	55-59	60-64	65-69	Total
Never smoked	33,255	32,959	27,817	21,892	115,884
Occasional only	11,823	11,705	10,339	7,913	41,781
Pipes only	8,498	11,057	11,906	11,580	43,041
Pipes and cigars	7,445	8,727	9,219	7,858	33,249
Cigars only	12,751	14,862	13,049	10,818	51,480
Cigarettes, pipes, and cigars	12,127	13,684	10,407	6,709	42,927
Cigarettes and cigars	10,302	10,229	6,925	4,644	32,099
Cigarettes and pipes	29,182	25,958	17,656	9,050	81,846
Cigarettes only	94,630	70,225	40,569	20,141	225,565
Total	219,913	190,367	147,888	100,605	657,753
Subtotals					
Cigarettes and other	51,511	49,871	34,988	20,403	156,773
All regular cigarette smokers	146,141	120,666	75,557	40,544	382,938

Haenszel, Shimkin, and Miller [2] have reported the results of a survey on smoking habits in a representative sample of the United States population conducted by the Census Bureau as a part of the Current Population Survey in February, 1955. They compared our findings with theirs for men in the same age range. According to their analysis, the two studies were in close agreement as to the proportion of men with a history of regular cigarette smoking.

Death Rates by Type of Smoking

Table 1 shows the number of man-years of exposure to risk by type of smoking (lifetime history) and by five-year age groups. Throughout this report, the age group always refers to the age of the smoked had the lowest death rate. Men with a history of regular cigarette smoking who also smoked cigars and pipes had a death rate some-

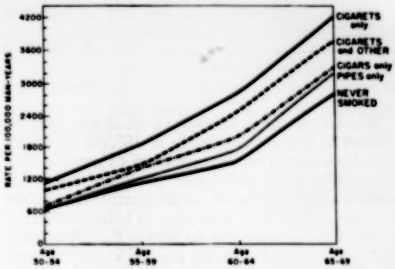

Fig. 1.—Total death rates by type of smoking (lifetime history) and by age at start of study.

what lower than that of men who smoked cigarettes only. The death rate of men who had smoked only pipes was just slightly above the rate for men who never smoked. The death rate of cigar smokers was slightly higher than that of pipe smokers.

In order to summarize these findings, we computed the number of deaths which would have occurred among men in each smoking category if their age-specific death rates had been exactly the same as those for men who never smoked. This will be referred to as the "expected" number of deaths. The observed number of deaths divided by the expected number gives the mortality ratio. By definition, the mortality ratio for men who never smoked is 1.00. In other words, the death rate of men who

TABLE 2.—*Total Deaths and Death Rates Per 100,000 Man-Years by Type of Smoking (Lifetime History) and by Age at Start of Study*

Type of Smoking	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Never smoked	218	656	375	1,139	438	1,575	613	2,800	1,644	1,644	1.00
Occasional only	88	744	174	1,659	191	1,851	243	3,071	696	595	1.09
Pipes only	52	612	139	1,257	200	1,755	374	3,230	774	694	1.12
Pipes and cigars	46	618	117	1,341	168	1,822	294	3,978	565	513	1.10
Cigars only	94	737	212	1,427	260	1,992	329	3,319	955	761	1.25
Cigarettes, pipes, and cigars	118	973	194	1,418	253	2,431	229	3,502	804	587	1.37
Cigarettes and cigars	97	951	144	1,408	171	2,469	163	3,510	575	422	1.36
Cigarettes and pipes	315	1,079	366	1,531	448	2,537	375	4,144	1,531	1,018	1.50
Cigarettes only	1,103	1,166	1,389	1,964	1,141	2,809	850	4,220	4,406	2,623	1.68
Total	2,131	969	3,007	1,568	3,282	2,220	3,450	3,479	11,870	8,858	1.34
Subtotals											
Cigarettes and other	550	1,029	731	1,466	872	2,492	777	3,808	2,910	2,028	1.43
All regular cigarette smokers	1,633	1,117	2,040	1,660	2,016	2,668	1,627	4,013	7,336	4,651	1.57

* Calculated by applying age-specific death rates of men who never smoked to man-years of exposure to risk of smokers in each category.

men at the time they were enrolled in 1952. Table 2 shows the corresponding number of deaths and death rates per 100,000 man-years.

In all four age groups, by far the highest death rate was that for men with a history of regular cigarette smoking only (fig. 1). Men who never never smoked is taken as a control against which the death rates of men in various smoking categories are compared (fig. 2).

A total of 4,406 deaths occurred among men with a history of regular cigarette smoking only. Only 2,623 of these men would have died between Jan-

uary, 1952, and October, 1955, had their age-specific death rate been the same as for men who never smoked. This difference of 1,783 deaths is statistically significant ($p<0.001$). The mortality ratio (4,406 ÷ 2,623) is 1.68. In other words, the

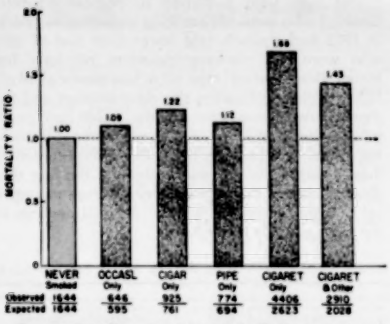

Fig. 2.—Mortality ratios for total deaths by type of smoking.

death rate of these cigarette smokers was 68% higher than the death rate of a comparable group of men who never smoked, age being taken into consideration.

The mortality ratio was 1.43 for men with a history of regular cigarette smoking who also smoked cigars or pipes, there being 2,910 observed against 2,028 expected deaths. This difference is statistically significant ($p<0.001$). It is interesting that these men with mixed smoking habits had somewhat lower death rates than men who smoked cigarettes

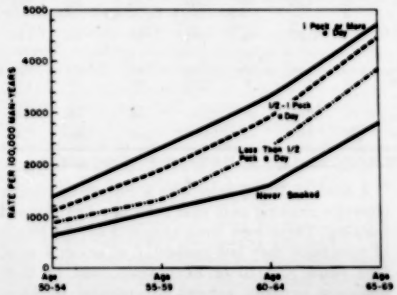

Fig. 3.—Total death rates by current amount of cigarette smoking at time of questioning and by age.

only. This is partly due to the fact that there were fewer heavy cigarette smokers among those with mixed habits than among those who smoked cigarettes only. However, this does not entirely account for the difference.

The mortality ratio was 1.22 for men with a history of cigar smoking only (925 observed deaths against 761 expected deaths). The difference is statistically significant ($p<0.001$). For men with a history of regular pipe smoking only, there were 774 observed deaths, compared with 694 expected deaths, giving a mortality ratio of only 1.12. While this difference is significant ($p<0.02$), the effect of pipe smoking seems to be small as compared with the effect of cigarette smoking.

646 deaths occurred among men with a history of occasional smoking as compared with 595 expected deaths. This difference is not statistically significant ($p=0.08$). It appears that occasional smoking has little, if any, effect on death rate.

Death Rates by Amount of Cigarette Smoking

The men with a history of regular cigarette smoking only were classified by their current amount of cigarette smoking at the time of questioning in 1952. In all four age groups the death rates increased markedly with amount of cigarette

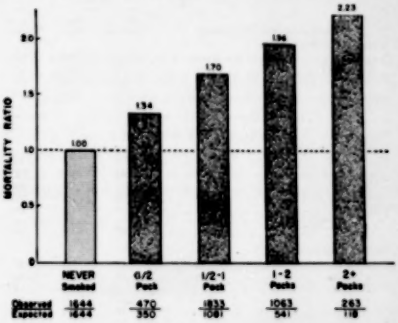

Fig. 4.—Mortality ratios for total number of deaths by current amount (1952) of cigarette smoking.

smoking (table 3 and fig. 3). The mortality ratio rose from 1.00 for men who never smoked to 1.34 for smokers of under one-half pack a day, to 1.70 for smokers of one-half to one pack a day, to 1.96 for smokers of one to two packs a day, and to 2.23 for smokers of two packs or more a day (fig. 4). In other words, the death rate of men smoking regularly at a rate of less than one-half pack of cigarettes a day was 34% higher than that of men who never smoked, the death rate of men smoking one to two packs a day was 96% higher than that of men who never smoked, and the death rate of men smoking two packs or more a day was 123% higher than that of men who never smoked.

The findings for men with a history of having smoked cigarettes regularly and pipes or cigars as well are shown in table 3 by amount of cigarette smoking in 1952. The amount of pipe and cigar

smoking of these men with mixed habits has been disregarded because (1) cigarette smoking appears to have far more effect on the death rate than pipe or cigar smoking and (2) we know of no meaningful way to convert number of cigars or number of pipefuls of tobacco into equivalent numbers of cigarettes. Again it is seen that the death rate increases with the amount of cigarette smoking but not quite so uniformly as for men with a history of cigarette smoking only. Holding the current amount of cigarette smoking constant, the men with mixed smoking habits had a death rate 11% lower than men with a history of cigarette smoking only. This was largely accounted for by men who were currently smoking both cigars and cigarettes in 1952, this group having a death rate 29% lower than that of men with a history of regular cigarette smoking only.

habit entirely or had cut down to occasional smoking. For comparison, table 4 also shows the number of deaths and death rates for men who were still smoking regularly in 1952 and for men who never smoked.

The men with a history of regular cigarette smoking who were not smoking cigarettes regularly in 1952 had a death rate lower than that of men who were still smoking cigarettes regularly but higher than that of men who had never smoked. What is more surprising, the cigar smokers and the pipe smokers who gave up the habit had death rates higher than those of men who were still smoking cigars or pipes regularly. The interpretation of these comparisons is complicated by the fact that illness is one of the reasons why a person may give up smoking. However, a more detailed analysis of the data clarifies the picture.

TABLE 3.—*Total Deaths and Death Rates Per 100,000 Man-Years by Amount of Smoking and by Age at Start of Study*

Daily Amount of Smoking	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Cigarette smoking only											
<½ pack	88	937	110	1,305	131	2,298	141	3,849	470	259	1.81
½-1 pack	443	1,378	551	1,875	487	2,975	357	4,441	1,833	1,081	1.70
1-2 packs	347	1,886	329	2,083	279	3,464	142	4,635	1,063	541	1.96
2+ packs	79	1,511	108	3,298	41	2,458	35	5,102	303	118	2.23
Uncertain	14	...	19	...	21	...	11	...	65	36	...
Total	966	1,215	1,108	1,930	964	2,806	686	4,350	3,694	2,125	1.74
Mixed Smoking											
<½ pack	62	948	85	1,116	138	2,491	119	3,967	494	317	1.57
½-1 pack	172	1,032	235	1,464	282	2,486	274	4,444	963	616	1.19
1-2 packs	116	1,350	144	1,822	134	2,871	93	4,110	487	287	1.70
2+ packs	28	1,466	35	2,474	22	2,469	14	3,431	99	51	1.82
Uncertain	3	..	10	...	8	...	17	...	38	36	...
Total	381	1,081	509	1,529	584	2,553	517	4,038	1,981	1,329	1.50
Cigar smoking only											
1-4 cigars	41	617	87	1,119	111	1,646	171	2,967	419	400	1.05
4+ cigars	30	789	69	1,731	63	1,951	67	2,940	229	185	1.24
Uncertain	1	...	3	...	3	...	7	...	14	13	...
Total	72	678	159	1,331	177	1,727	245	2,970	653	598	1.09
Pipe smoking only											
1-10 pipefuls	30	472	58	1,095	98	1,545	215	3,309	391	374	1.05
10+ pipefuls	30	782	46	1,466	66	2,255	72	2,745	304	172	1.19
Uncertain	2	...	3	...	4	...	5	...	14	13	...
Total	42	606	107	1,194	168	1,762	292	3,130	609	560	1.09
Nonsmokers	218	656	375	1,139	438	1,575	613	2,800	1,644	1,644	1.00

* Calculated by applying age-specific death rates of men who never smoked to man-years of exposure to risk of smokers in each category.

The death rates of cigar smokers who smoked no more than 4 cigars a day and of pipe smokers who smoked no more than 10 pipefuls of tobacco a day differed very little from the death rate of men who never smoked. However, cigar smokers and pipe smokers who smoked more than this amount had death rates significantly higher than men who never smoked ($p<0.005$ for cigar smokers and $p=0.05$ for pipe smokers).

Death Rates for Exsmokers

Table 4 shows the number of deaths and death rates for men with a history of regular smoking who said in 1952 that they either had given up the

A total of 10,095 men with a history of regular cigarette smoking only said that they had stopped smoking. These men were classified by the length of time since they last smoked, i. e., under 1 year, 1-10 years, and 10 or more years, and by their maximum previous amount of cigarette smoking, i. e., under one pack a day and one pack or more a day (fig. 5). Those who said that they had stopped smoking cigarettes less than a year before they were questioned had a higher death rate than those who were still smoking. In our opinion, this reflects the effect of health on smoking habits rather than the reverse; that is, some people give up

smoking only because they are ill. There were probably some such men among those who had stopped smoking less than a year before the study was begun. This would account for the high death rate in this group. However, men who had stopped smoking for a year or longer had a lower death rate than those who continued to smoke regularly.

The mortality ratio was 1.61 for men who were currently smoking less than one pack a day of cigarettes in 1952. Mortality ratios for exsmokers who had previously smoked at this level were (1) 2.04 for those who had stopped smoking for less than one year, (2) 1.30 for those who had stopped smoking for 1 to 10 years, and (3) 1.08 for those who had stopped smoking for 10 years or longer. The drop in the mortality ratio from 1.61 to 1.08 is statistically significant ($p<0.001$).

The mortality ratio was 2.02 for men who were currently smoking one pack or more a day of cigarettes in 1952. The mortality ratios for exsmokers who had previously smoked at this level were (1) 2.69 for those who had stopped smoking for less than one year, (2) 1.82 for those who had stopped smoking for 1 to 10 years, and (3) 1.50 for those who had stopped smoking for 10 years or longer. The drop in the mortality ratio from 2.02 to 1.50 is statistically significant ($p<0.02$).

Cigar smokers who had given up the habit less than a year before the questioning also had a high death rate. The rate dropped for those with more than a year of abstinence but remained relatively high. The picture for pipe smokers was roughly the same.

Death Rates for Those Who Reduced Amount of Smoking

A considerable number of men with a history of regular cigarette smoking only smoked cigarettes regularly in 1952 but had cut down on their consumption of cigarettes. The following three sets of comparisons show mortality ratios in relation to change in the amount of cigarette smoking. The first comparison indicates that (1) for those currently smoking one-half pack or more of cigarettes a day the mortality ratio was 1.82 (3,159 observed deaths and 1,740 expected deaths), (2) for those currently smoking less than one-half pack of cigarettes a day who had cut down from a higher amount the mortality ratio was 1.71 (133 observed deaths and 78 expected deaths), and (3) for those currently smoking less than one-half pack of cigarettes a day who had never regularly smoked any higher amount the mortality ratio was 1.24 (337 observed deaths and 272 expected deaths).

The second comparison indicates that (1) for those currently smoking one pack or more of cigarettes a day the mortality ratio was 2.02 (1,326

TABLE 4.—*Total Deaths and Death Rates Per 100,000 Man-Years by History of Regular Smoking in Relation to Current Smoking in 1952 and by Age at Start of Study*

History of Regular Smoking	Current Smoking in 1952	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Cigarettes only	None†	123	915	180	1,526	179	2,457	143	3,796	625	428	1.46
	Occasional†	14	842	21	1,547	31	3,010	21	3,493	87	60	1.45
	Regular†	906	1,215	1,108	1,909	934	2,896	686	4,359	3,694	2,125	1.74
Cigarettes and other	None†	139	957	172	1,586	240	2,466	307	3,361	739	561	1.32
	Occasional†	29	779	50	1,570	48	2,613	53	3,678	180	139	1.29
	Regular†	381	1,661	509	1,589	584	2,553	517	4,068	1,991	1,329	1.50
Cigars only	None‡	17	1,119	39	1,817	63	3,081	86	4,379	305	122	1.68
	Occasional‡	5	824	14	1,805	30	2,649	28	4,621	67	42	1.60
	Regular‡	72	678	159	1,331	177	1,727	245	2,970	653	598	1.09
Pipes only	None§	8	636	30	1,675	39	1,849	75	3,509	152	115	1.32
	Occasional§	2	629	2	665	2	766	7	2,201	13	19	0.68
	Regular§	42	606	107	1,194	168	1,702	292	3,159	649	560	1.09
Never smoked	None	218	656	375	1,139	458	1,575	613	2,809	1,644	1,644	1.00

* Calculated by applying age-specific death rates of men who never smoked to man-years of exposure to risk of smokers in each category.
† Cigarette smoking.
‡ Cigar smoking.
§ Pipe smoking.

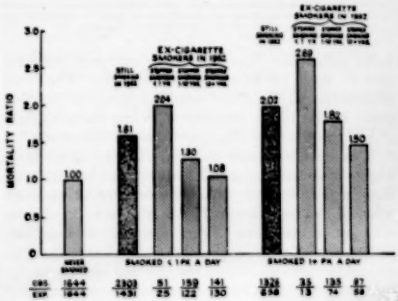

Fig. 5.—Mortality ratios for total number of deaths of men who had stopped smoking cigarettes compared with those for men who never smoked and those for men still smoking cigarettes in 1952.

observed deaths and 658 expected deaths), (2) for those currently smoking one-half to one pack of cigarettes a day who had cut down from a higher amount the mortality ratio was 1.96 (239 observed deaths and 122 expected deaths), and (3) for those currently smoking one-half to one pack of cigarettes a day who had never regularly smoked any higher amount the mortality ratio was 1.66 (1,594 observed deaths and 959 expected deaths).

The third comparison indicates that (1) for those currently smoking two or more packs of cigarettes a day the mortality ratio was 2.23 (263 observed deaths and 118 expected deaths), (2) for those currently smoking one to two packs of cigarettes a day who had cut down from a higher amount the mortality ratio was 3.16 (142 observed deaths and 45 expected deaths), and (3) for those currently smoking one to two packs of cigarettes a day who had never regularly smoked any higher amount the mortality ratio was 1.86 (921 observed deaths and 495 expected deaths).

As shown above, those who had smoked two or more packs of cigarettes a day and who had cut down to one to two packs a day had a higher mortality ratio than those who were currently smoking two or more packs of cigarettes a day. The most reasonable explanation would appear to be that some of the heavy smokers who cut down slightly did so because of illness or serious symptoms.

The mortality ratio of men who cut down from higher amounts to one-half to one pack of cigarettes a day was a trifle lower than the mortality ratio of men who did not cut down. The mortality ratio of men who cut down from higher amounts to less than one-half pack a day was appreciably lower than the mortality ratio of those who did not cut down.

All things considered, these figures suggest that cutting down from a high amount to a low amount of cigarette smoking results in a reduction of the death rate. Unfortunately, data are not available to make a more detailed analysis by time relationships, as was done in the case of men who stopped smoking altogether.

Duration of Smoking

Of the men with a history of regular cigarette smoking only who in 1952 were smoking regularly, 59% said that they began smoking when they were under 20 years old, 33.8% said that they began when they were in their 20's, and only 7.2% said that they began when they were 30 years old or older. The amount of smoking in 1952 seemed to be somewhat related to the ages at which the men began smoking. For example, only 32.7% of those who smoked one pack or more of cigarettes a day began smoking after the age of 19. By comparison, 54.1% of those who smoked less than one-half pack a day began smoking after the age of 19. The men in the age groups 50-54 and 55-59 began smoking at a somewhat younger age, on the average, than the men in the age groups 60-64 and 65-69.

Those who had smoked cigarettes regularly, but who had stopped smoking, had, on the average, started smoking at about the same ages as men who were smoking cigarettes regularly in 1952. For example, 40% of those who had stopped smoking started smoking after the age of 19. By comparison, 41% of those currently smoking cigarettes regularly had started smoking after the age of 19. Men with mixed smoking habits (i. e., cigarette and other) began smoking cigarettes at just about the same ages as men who smoked cigarettes only.

TABLE 5.—*Observed Versus Expected* Number of Deaths by Current Amount of Cigarette Smoking and by Years of Cigarette Smoking†*

Amount Per Day	Deaths by Duration of Smoking, Yr.								
	<25			25-34			35+		
	Observed	Expected	Ratio	Observed	Expected	Ratio	Observed	Expected	Ratio
<½ pack	62	56	1.11	114	88	1.30	286	201	1.42
½-1 pack	123	83	1.48	458	262	1.75	1,226	721	1.70
1-2 packs	55	26	2.12	253	130	1.95	746	378	1.97
2+ packs	6	4	...	53	25	2.12	203	85	2.39

* Calculated by applying age-specific death rates of men who never smoked to man-years of exposure to risk of smokers in each category.
† Men with history of regular cigarette smoking only. Men who did not state amount or duration of smoking are omitted from table.

Table 5 shows the number of observed and expected deaths and mortality ratios for men with a history of regular cigarette smoking only by current amount of smoking and by years of smoking. There appears to be an upward trend in mortality ratios with years of smoking for men currently smoking less than one-half pack of cigarettes a day. Some of these men had previously smoked more than one-half pack a day and then cut down to less. Among men smoking one-half to one pack of cigarettes a day, the mortality ratio was less for those who had smoked less than 25 years than for those who had smoked 25 years or longer, but the difference is not statistically significant. The mortality ratios do not appear to be related to the years of smoking of men currently smoking one pack or more of cigarettes a day. Unfortunately, there are not enough cases to make a detailed analysis of the three variables: (1) years of smoking, (2) current amount of smoking, and (3) maximum amount of smoking. For this reason, one should be cautious in interpreting these figures.

Urban Versus Rural

The men were classified into the following four groups according to the addresses given on the smoking questionnaires collected in 1952: 1. Cities of over 50,000 population. This included men from Los Angeles, San Francisco, Minneapolis, Chicago, Detroit, Buffalo, Rochester, Syracuse, Pittsburgh, Newark, and other large cities. 2. Cities of 10,000 to 50,000 population. 3. Towns and suburbs. This is a mixed group of men living in towns of 2,500 to 10,000 population and men living in towns or rural areas in metropolitan counties as defined in the 1950 census of the United States. Undoubtedly, many of these men live in a small town but commute to work in a large city. 4. Rural areas. This group consisted of men with rural route addresses in nonmetropolitan counties and towns of under 2,500 population in nonmetropolitan counties.

We were unable to classify 2,241 of the men in this way because their addresses were not satisfactory for the purpose.

Table 6 shows the percentage distribution of the initial population in each of the groups by smoking habits and by age, and table 7 shows the number of deaths and death rates by smoking habits for each of the four areas described above. Since each of these groups is only about one-fourth the total population, we combined several smoking categories in order to obtain more stable rates. The age-specific death rate of the combined group (those who never smoked and those who smoked occasionally only) was used as a basis for computing the expected number of deaths and mortality ratios.

Regardless of type of locality, cigarette smokers had a much higher death rate than men who had not smoked regularly. This was true in all four age groups in all four areas. With the age-specific death rate of the combined group used as a basis for comparison, the mortality ratios for the cigarette smokers were almost identical in three of the four areas. The mortality ratios were higher among men living in cities of 10,000 to 50,000 population than among men in the other areas, but the difference in mortality ratios is not statistically significant ($p=0.63$).

Death rates in rural areas of the United States generally tend to be somewhat lower than death rates in cities.[3] Disregarding smoking habits, the total death rate was lower in the rural area than in cities of 50,000 or more population in three of the four age groups. Standardized to the age distribution of the 1954 computation of the white male population of the United States, the death rate for men in the rural area was 1,769 per 100,000 per year, as compared with 1,931 per 100,000 per year for men in cities of 50,000 or more population, a difference of 9.2%. However, there was a smaller proportion of cigarette smokers and a larger proportion of men who never smoked or smoked only occasionally in rural areas than in large cities (table 6), Haenszel, Shimkin, and Miller [2] also found this to be true for the United States as a whole. Standardizing the figures for smoking habits as well as for age, the death rate was 1,820 in the rural group, as compared with 1,884 in cities of 50,000 or more population, a difference of only 3.5%. In other words, about three-fifths of the difference in age-standardized death rates between the rural population and the large city population disappeared when smoking habits were equated.

TABLE 6.—*Man-Years of Exposure to Risk, Initial Number of Men, and Percentage Distribution of Initial Population by Smoking Habits for Each of Four Areas*

	Age Group, Yr.				
	50-54	55-59	60-64	65-69	Total
Cities of Over 50,000 Population					
Man-years	55,855	49,392	34,266	21,275	160,788
Initial No. of men	15,481	13,831	9,722	6,184	45,218
Never smoked or occasional only, %	16.8	18.1	20.5	22.8	18.8
Cigars and pipes %	13.3	17.4	22.8	28.8	18.7
Cigarettes, %*	69.9	64.4	57.0	48.4	62.5
Cigarettes, 1 pack or more a day, %*	21.1	16.7	12.3	8.2	16.1
Cities of 10,000 to 50,000 Population					
Man-years	52,160	46,919	33,549	22,038	154,666
Initial No. of men	14,481	13,146	9,504	6,371	43,502
Never smoked or occasional only, %	18.9	19.5	23.1	27.1	21.2
Cigars and pipes %	12.5	17.8	22.0	29.6	18.7
Cigarettes, %*	68.5	62.7	54.9	43.3	60.1
Cigarettes, 1 pack or more a day, %*	19.4	14.5	10.2	6.5	14.0
Towns and Suburbs					
Man-years	58,783	52,342	39,298	27,467	177,930
Initial No. of men	16,293	14,657	11,132	7,957	50,039
Never smoked or occasional only, %	20.3	22.0	25.4	29.8	23.4
Cigars and pipes, %	13.8	17.6	23.5	30.5	19.7
Cigarettes, %*	66.0	60.4	51.2	39.7	56.9
Cigarettes, 1 pack or more a day, %*	18.6	14.4	10.1	6.4	13.5
Rural					
Man-years	59,592	48,880	38,824	28,759	166,845
Initial No. of men	14,000	13,524	10,979	8,280	46,783
Never smoked or occasional only, %	36.0	29.3	32.5	35.7	30.2
Cigars and pipes, %	12.2	16.6	23.5	30.7	19.4
Cigarettes, %*	61.7	54.1	43.9	33.5	50.4
Cigarettes, 1 pack or more a day, %*	15.7	11.0	7.9	5.0	10.6

*Includes men who smoked cigars or pipes as well as cigarettes.

Analysis by States

An analysis of death rates by smoking habits has been made separately for each of the nine states in which the study was conducted. Smoking groups were combined in the same way as previously described for the urban-rural analysis. In all four age groups in each of the nine states the death rate of men with a history of regular cigarette smoking was higher than the death rate of men who had never smoked or smoked only occasionally. Likewise, the death rate of smokers of one pack or more of cigarettes a day was consistently higher

than the death rate of men who smoked cigarettes but in lesser amounts. Comparing the combined group with smokers of one pack or more of cigarettes a day, the mortality ratios by state were as follows: California, 2.21; Illinois, 2.02; Iowa, 2.18; Michigan, 1.73; Minnesota, 1.60; New Jersey, 2.20; New York, 1.85; Pennsylvania, 1.70; and Wisconsin, 1.72. This variation is no greater than would be expected considering the size of the samples ($p=0.45$).

Comparison of Study Periods

One of the purposes of continuing the study for another two years after the publication of our first findings was to determine whether any appreciable changes would occur in the mortality ratios (i. e., close in the two periods, except that the mortality ratios for smokers were in general a trifle higher in the last two years than in the earlier period. However, the differences are not statistically significant.

Independent Check on Follow-up

We anticipated that some of the volunteer researchers might be inclined to assume that the subjects (most of whom were close friends or relatives) were alive until they heard to the contrary. This difficulty was most likely to arise in the case of subjects who moved. As a safeguard, we asked the researchers to record all changes of address.

In order to make an independent check of the follow-up work done by the researchers, we selected a sample of 38,583 men from three groups:

TABLE 7.—*Total Deaths and Death Rates per 100,000 Man-Years by Smoking Habits, by Age at Start of Study, and by Area*

Area and Smoking Category	Age Group, Yr. 50-54 No. of Deaths	50-54 Death Rate	55-59 No. of Deaths	55-59 Death Rate	60-64 No. of Deaths	60-64 Death Rate	65-69 No. of Deaths	65-69 Death Rate	Observed Vs. Expected* No. of Deaths Observed	Expected	Ratio
Cities, 50,000+ population											
Never smoked or occasional only	54	574	120	1,337	126	1,703	140	2,858	440	440	1.00
Cigars, pipes	40	533	115	1,332	155	1,974	180	3,057	490	476	1.05
Cigarettes†	424	1,089	507	1,505	533	2,750	447	4,385	1,911	1,287	1.48
Total	518	927	742	1,502	814	2,376	776	3,648	2,850	2,203	1.29
Cigarettes, 1+ packs†	155	1,205	106	2,067	144	3,483	83	4,787	546	300	1.82
Cities, 10,000-50,000 population											
Never smoked or occasional only	62	633	109	1,181	128	1,635	130	2,477	449	449	1.00
Cigars, pipes	51	779	102	1,213	137	1,842	212	3,243	502	424	1.18
Cigarettes†	418	1,172	521	1,779	471	2,577	376	3,981	1,786	1,103	1.62
Total	531	1,018	732	1,560	736	2,194	718	3,349	2,737	1,974	1.39
Cigarettes, 1+ packs†	148	1,471	102	2,417	97	2,859	55	3,849	402	293	1.38
Towns and suburbs											
Never smoked or occasional only	89	744	123	1,062	108	1,671	256	3,125	628	628	1.00
Cigars, pipes	53	652	132	1,428	179	1,930	261	3,092	625	577	1.08
Cigarettes†	436	1,127	549	1,742	508	2,544	454	4,294	1,947	1,294	1.50
Total	578	983	804	1,596	855	2,176	973	3,529	3,210	2,500	1.28
Cigarettes, 1+ packs†	146	1,344	102	2,176	115	2,944	85	4,019	508	279	1.82
Rural											
Never smoked or occasional only	99	750	143	1,002	193	1,514	297	2,879	732	732	1.00
Cigars, pipes	45	726	112	1,392	160	1,737	287	3,367	634	539	1.18
Cigarettes†	335	1,077	430	1,651	472	2,799	322	3,346	1,559	1,027	1.52
Total	479	949	685	1,416	825	2,125	916	3,185	2,905	2,279	1.27
Cigarettes, 1+ packs†	109	1,381	107	2,025	92	3,056	54	3,827	302	199	1.52

* Calculated by applying age-specific death rates of men who never smoked or who smoked occasionally only to man-years of exposure to risk of smokers in each category.

† Includes men who smoked cigars or pipes as well as cigarettes.

the death rates of smokers are compared with the death rate of nonsmokers). As of the cut-off date for receiving data presented in our first report, the volunteers had reported 4,854 deaths occurring in the period from January, 1952, through October, 1953. Subsequent information received from the volunteers raised this to a total of 5,066. They reported 6,804 deaths which occurred during the next two years (i. e., from November, 1953, through October, 1955). Table 8 shows the number of deaths and death rates for each of these two periods for several smoking categories. The relationships between smoking habits and death rates were quite

(1) a representative sample of 60% of the men who said that they had never smoked, (2) all of the men with a history of regular cigarette smoking only who were currently smoking one to two packs of cigarettes a day in 1952, and (3) all of the men who were currently smoking two or more packs of cigarettes a day in 1952. For the sake of brevity, we refer to these last two groups combined as "heavy cigarette smokers." In the first week of November, 1955, we mailed a brief questionnaire (asking current cigarette smoking habits and date of birth) to all of these subjects except those whom we knew to be dead. The following request

was printed on the face of the questionnaire: "If the man whose name appears on the other side of this card is dead, check here and return this card." In order to obtain as complete coverage as possible, five successive mailings were used, the last being certified mail requiring that the addressee sign a receipt card which was returned to us by the post office. By the end of this mailing process, we had obtained information on all but 2,135 of the 38,583 men in the sample. Records on these 2,135 men were sent to the respective divisions of the American Cancer Society for further checking, and 1,428 of them were found. Thus, 37,876 of the men were successfully traced (98.2% of the sample). Independently of this, the volunteers sent us routine follow-up reports on these men, together with reports on all the other men in the study.

searchers are as close as could be expected on the basis of sampling variation ($p=0.38$). Furthermore, the failure of the volunteers to report some deaths had only a trivial effect on the mortality ratios, as indicated by the following comparisons.

First, we applied the age-specific death rate for men who never smoked to the man-years of exposure to risk of heavy cigarette smokers, considering only the reports submitted by the volunteers. This gave 1,425 observed deaths versus 712 expected deaths, a mortality ratio of 2.00. Next, we carried out the same procedure, including all deaths but including as alive only those so reported both by volunteers and by independent tracing. This gave 1,497 observed deaths versus 744 expected deaths, a mortality ratio of 2.01. Finally, we considered all cases traced by either one of the

TABLE 8.—*Comparison of Total Deaths and Death Rates Per 100,000 Man-Years for Selected Smoking Categories by Age at Start of Study in Periods January, 1952, through October, 1953, and November, 1953, through October, 1955*

Smoking Category	Age Group, Yr.								Observed Vs. Expected* No. of Deaths		
	50-54		55-59		60-64		65-69				
	No. of Deaths	Death Rate	No. of Deaths	Death Rate	No. of Deaths	Death Rate	No. of Deaths	Death Rate	Observed	Expected	Ratio
Jan., 1952-Oct., 1953											
Never smoked	93	611	159	1,051	171	1,332	285	2,784	708	708	1.00
Pipes only	24	618	58	1,140	83	1,507	102	2,983	327	302	1.08
Cigars only	42	719	86	1,254	108	1,785	156	3,669	392	330	1.19
Cigarettes and other	230	930	319	1,586	302	2,220	319	3,311	1,220	872	1.40
1+ packs a day	52	1,010	78	1,816	65	2,460	41	3,220	236	147	1.61
Cigarettes only	451	1,036	571	1,756	520	2,740	509	3,866	1,911	1,126	1.70
1+ packs a day	170	1,233	181	2,082	119	2,765	70	3,906	540	283	1.91
Total	883	875	1,288	1,411	1,300	2,022	1,466	3,159	5,066	3,817	1.33
Nov., 1953-Oct., 1955											
Never smoked	125	606	216	1,214	267	1,782	328	2,814	936	936	1.00
Pipes only	28	607	81	1,357	126	1,970	212	3,447	447	392	1.14
Cigars only	52	853	126	1,574	152	2,172	260	3,540	533	431	1.24
Cigarettes and other	310	1,113	412	1,584	510	2,730	458	4,254	1,690	1,155	1.46
1+ packs a day	92	1,503	101	2,029	91	3,077	66	4,698	350	195	1.79
Cigarettes only	652	1,276	738	1,957	624	2,899	481	4,540	2,495	1,495	1.67
1+ packs a day	251	1,558	247	2,470	181	3,738	107	5,451	786	375	2.10
Total	1,218	1,049	1,709	1,592	1,892	2,391	1,955	3,939	6,804	5,038	1.35

* Calculated by applying age-specific death rates of men who never smoked to man-years of exposure to risk of smokers in each category.

We found that there was a time lag in the reporting of some deaths by the volunteers. Usually about 7% of the deaths were reported one follow-up later than they should have been reported. The volunteers missed less than 3% of deaths which they had had two or more opportunities to report. For the entire period, the underreporting of deaths by the volunteers amounted to only 5.1%. The most important finding of this checking procedure was that failure of the volunteers to report some deaths was unrelated to the smoking habits of the men.

A total of 1,031 deaths occurred among men who never smoked, of which 973 (94.4%) were reported by the volunteers and 58 (5.6%) were found by independent tracing. A total of 1,497 deaths occurred among the heavy cigarette smokers, of which 1,425 (95.2%) were reported by the volunteers and 72 (4.8%) were found by independent tracing. The percentages of deaths not reported by the re-

two procedures. This gave 1,497 observed deaths versus 752 expected deaths, a mortality ratio of 1.99.

Time Trends.—Table 9 shows the comparison of death rates for men who never smoked and for heavy cigarette smokers with the death rate for white males in the United States in two periods of time: January, 1952, through October, 1953, and November, 1953, through October, 1955. The figures for males in the United States have been adjusted for aging of the population and for seasonal variation. The figures in this study include all the men traced by the volunteers, by independent tracing, or by both.

The death rate of the men who never smoked was far lower than the death rate in the United States in all four age groups in both periods of time. The ratio of the death rate of men who never smoked to the death rate in the United States rose somewhat with time in all four age groups.

The death rate of the heavy cigarette smokers was slightly less than the rate in the United States in three of the four age groups in the first time period. However, in the second time period the death rate of the heavy cigarette smokers was higher than the rate for white males in the United States by amounts ranging from 7% in the age group 65-69 to 19% in the age group 55-59. The reason for the relative rise in death rates of the study population will be discussed later in this report.

Age.—It is well known that age, as recorded on death certificates, is not always correct; therefore, we were not surprised to find that the age as recorded on the death certificate did not always agree with the age entered on the smoking questionnaire in 1952. We also found some differences between age as recorded on the original questionnaire in 1952 and date of birth as recorded on the mailed questionnaire used for the independent check on follow-up.

In order to determine whether discrepancies in the recording of age could have had any appreciable effect on the results of the study, we computed

TABLE 9.—*Comparison of Death Rates per 100,000 Man-Years of Men Who Never Smoked and of Heavy Cigarette Smokers by Age at Start of Study With That of Equivalent White Male Population of United States*

	Age Group, Yr.			
	50-54	55-59	60-64	65-69
Jan. 1952-Oct. 1953				
1. Death rate: never smoked	656	1,016	1,365	2,013
2. Death rate: heavy cigarette smokers	1,222	2,140	2,767	3,856
3. Death rate: U. S. white males	1,288	2,006	2,991	4,354
Ratio: 1 ÷ 3	0.51	0.51	0.46	0.60
Ratio: 2 ÷ 3	0.95	1.07	0.93	0.89
Ratio: 2 ÷ 1	1.86	2.11	1.98	1.48
Nov. 1953-Oct. 1955				
1. Death rate: never smoked	777	1,253	1,781	3,280
2. Death rate: heavy cigarette smokers	1,659	2,632	4,031	5,246
3. Death rate: U. S. white males	1,439	2,210	3,402	4,895
Ratio: 1 ÷ 3	0.54	0.57	0.52	0.67
Ratio: 2 ÷ 3	1.15	1.19	1.18	1.07
Ratio: 2 ÷ 1	2.14	2.10	2.26	1.60

the mortality ratio of heavy cigarette smokers as compared to men who never smoked in three different ways. First, we made an analysis including all traced subjects and assuming that the original statement of age was correct. This gave a mortality ratio of 1.99. Second, we made an analysis confined to those cases where the information on the mailed questionnaire or death certificate was in agreement with the age as originally stated. This was true of 89% of the cases. The mortality ratio was 2.07. Finally, we made an analysis assuming that the information on the mailed questionnaire or death certificate was correct regardless of the age recorded on the original questionnaire. This also gave a mortality ratio of 2.07.

As shown above, the analysis based on the assumption that the original statement of age was correct gave the lowest mortality ratio. Therefore, it appears that if there was a small systematic bias in age as originally stated, it was in such a direction as to produce an underestimate of the degree of association between death rate and heavy cigarette smoking.

Second Independent Check on Follow-up.—To make doubly sure that no error was introduced by underreporting of deaths, all of the subjects with New Jersey addresses were checked against the entire list of deaths occurring in the state of New Jersey in 1954 and 1955. This was accomplished through the cooperation of Dr. Marguerite F. Hall, Director of the Division of Vital Statistics and Administration of the New Jersey State Department of Health. Among those subjects previously traced in two ways, no deaths were found which were not either reported by the volunteers or discovered in the mail tracing.

Effect of Screening Out Ill Men

In retrospective studies of habits in relation to disease, subjects are not questioned until after they become ill. Conceivably, illness could bias the way in which a person answers questions about his habits. In designing this prospective study, we sought to avoid this possibility. It was for this reason that we instructed the volunteers not to enroll a man if they knew he had lung cancer or if he was seriously ill from any disease. Obviously, this procedure was not as efficient as screening prospective subjects by medical examinations (which was not feasible). Nevertheless, the results indicate that the volunteers were conscientious in carrying out their instructions. This is shown by the following figures.

Only 24 of the 187,783 men died within one week after they were questioned; 38 died in the second week, 36 in the third week, 46 in the fourth week, and 45 in the fifth week. Of the 24 who died in the first week, none died of cancer, 16 of heart attacks, 3 of cerebral hemorrhage, and 5 of various other causes. Only 12 men died of cancer within one month after they were questioned; 19 died in the second month, 27 in the third month, 30 in the fourth, and 35 in the fifth month. Deaths occurring in the first several weeks were predominantly due to relatively sudden causes (e. g., heart attacks, strokes, and accidents). Although a few men died of cancer within a short time after they were questioned, a study of the records indicates that it is unlikely that the volunteers who enrolled them knew that they had cancer. For example, one man had a thoracotomy nine days after he was enrolled in the study. It was found that he had lung cancer, and he died five days later.

The exclusion of seriously ill men naturally resulted in very low death rates in the early part of the study. It is generally agreed by actuaries that the selective effect of screening out sick persons by medical examination is great during the first year, diminishes rapidly with time, is relatively

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slight after the third year, and for all practical purposes wears off within five years. Mr. Edward A. Lew of the Metropolitan Life Insurance Company gave us the figures (from intercompany studies) for men in the age group 55-59 who purchased standard ordinary life insurance in 1951-1953. The death rate rose from 407 per 100,000 men in the first year after purchase of insurance to 647 the next year, an increase of 59%. By comparison, the death rate of our subjects in the same age group was 1,215 per 100,000 men in the period January-October, 1952, and rose to 1,600 the next year, an increase of only 32%. We conclude that the screening out of ill men by our volunteers was far less efficient than the medical screening applied to applicants for standard life insurance. By the same token, there is reason to believe that the effect of screening by our volunteers wore off more rapidly. Volunteers would be unaware of nonsymptomatic conditions which a physician would find.

In the first time period, the death rate of men in the study was far below the comparable rate for the United States population (i. e., only about 64% of the latter rate). We attribute this to the fact that ill men were largely excluded by the volunteers. However, the death rate rose rapidly with time as the effect of this selection wore off. In the last year of the study (November, 1954, through October, 1955), the rate for our study group was 82% of the rate for the white male population of the United States in the age group 50-54, 81% in the age group 55-59, 78% in the age group 60-64, and 84% in the age group 65-69.

As previously described, there is reason to suppose that the effect of screening out ill men had nearly worn off by the last year of the study. Therefore, it appears that the death rate of our study in the same period of time, and the corresponding rates for men who had held standard ordinary life insurance policies for 5 to 15 years.

TABLE 10.—*Comparison of Death Rate per 100,000 Man-Years of Men in This Study* by Age at Start of Study with that of Total White Male Population of United States and that of Equivalent Holders of Standard Ordinary Life Insurance†*

Period and Population Group	Age Group, Yr.							
	50-54		55-59		60-64		65-69	
	Death Rate	Ratio to U. S. Rate	Death Rate	Ratio to U. S. Rate	Death Rate	Ratio to U. S. Rate	Death Rate	Ratio to U. S. Rate
Jan. 1952-Oct. 1952								
Study group	778	0.64	1,215	0.64	1,698	0.61	2,700	0.66
Life insurance holders	770	0.64	1,156	0.61	1,601	0.57	2,618	0.64
U. S. white males	1,225	1.00	1,899	1.00	2,789	1.00	4,070	1.00
Nov. 1952-Oct. 1953								
Study group	974	0.73	1,600	0.77	2,324	0.74	3,601	0.79
Life insurance holders	842	0.63	1,207	0.58	1,773	0.57	2,618	0.58
U. S. white males	1,331	1.00	2,080	1.00	3,132	1.00	4,553	1.00
Nov. 1953-Oct. 1954								
Study group	1,027	0.75	1,565	0.74	2,375	0.73	3,594	0.77
Life insurance holders	914	0.66	1,326	0.63	1,847	0.57	2,738	0.59
U. S. white males	1,375	1.00	2,111	1.00	3,245	1.00	4,679	1.00
Nov. 1954-Oct. 1955								
Study group	1,233	0.82	1,864	0.81	2,773	0.78	4,315	0.84
Life insurance holders	940	0.63	1,363	0.59	2,057	0.58	2,801	0.55
U. S. white males	1,502	1.00	2,308	1.00	3,559	1.00	5,111	1.00

* Death rates of study population corrected for underreporting of deaths by volunteers.
† Death rates for males who had held standard ordinary life insurance policies for from 5 to 15 years; information provided by Mr. Edward A. Lew of the Metropolitan Life Insurance Company from intercompany studies.

In the last year of the study the age-specific death rate of our study population was about 87% of that of the general white male popu-

Comparison with Death Rates in the United States

The independent check on follow-up (as previously described) revealed that the volunteers failed to report 5.1% of the deaths which actually occurred. The percentage of additional deaths not reported by the volunteers was 1.2% for the period of January, 1952, through October, 1952; 3% for the period of November, 1952, through October, 1953; 3.5% for the period of November, 1953, through October, 1954; and 11.4% for the period of November, 1954, through October, 1955. Table 10 shows the death rates by age for all the men in the study by time periods, the rates being adjusted for underreporting of deaths by the percentages given above. Also shown for comparison is the death rate of white males in the United States of the same age population would stabilize at about 81% to 85% of the rate for white males in the general United States population. This relatively small difference is partially accounted for by the following facts.

The study was carried out in 394 counties. We applied the age-specific death rate for the white male population in each of these counties in 1950 to the number of subjects selected from each and summed the results. The death rates were below those for white males in the United States in 1950 by the following amounts: 5.6% in the age group 50-54, 4.2% in the age group 55-59, 3.3% in the age group 60-64, and 2.9% in the age group 65-69. Adjusting the figures given earlier by these amounts, it appears that in the last year of the study the age-

lation in the study area in the age group 50-54, about 84% in the age group 55-59, about 81% in the age group 60-64, and about 87% in the age group 65-69.

The remaining difference is probably attributable to a slight degree of socioeconomic selection and to the fact that the volunteers did not enroll men who were for a long-term stay in such institutions as mental hospitals and tuberculosis sanatoriums. Neither did they enroll itinerant laborers and similar groups that could not have been traced.

The fact that the socioeconomic selection of our study population was relatively slight is indicated by this comparison. As shown in table 10, the death rate of men who had held standard ordinary life insurance policies for 5 to 15 years was only 63% of the rate for the white male population of the United States in the age group 50-54 and only 55% of that in the age group 65-69 in the period of November, 1954, through October, 1955. These men had held life insurance policies long enough for the effect of medical selection to wear off. Their death rates were far lower than the rates of our study population. Holders of standard ordinary life insurance policies, are largely persons in the middle and upper economic strata, and such insurance is not sold to people in dangerous occupations, to people with questionable habits, or to people with impairments thought to have an effect on mortality.

The slight socioeconomic selection of our subjects could have had no influence on the findings of this study unless the distribution by socioeconomic class differed markedly among the cigarette smokers as compared with the men who did not smoke cigarettes. According to Moriyama and Guralnick,[4] among men in the age group 55-64 the following relation of death rates to socioeconomic class (as indicated by occupation level) is found: 1. Agricultural workers, including farm owners, have the lowest death rate. 2. Occupation levels 1 and 2, comprising professional, technical, administrative, and managerial workers, have a death rate about 9% higher than agricultural workers. 3. Occupation levels 3 and 4, comprising proprietors and clerical, sales, skilled, and semiskilled workers have a death rate about 8% higher than that of workers in levels 1 and 2. 4. Occupation level 5, comprising laborers have a death rate about 47% higher than that of workers in levels 1 and 2.

Three states (California, New Jersey, and Pennsylvania) supplied us with photostatic copies (rather than abstracts) of death certificates, and we classified men aged 50-64 who died in these states by occupation level. The results were as follows: 24% of the cigarette smokers and 29% of the men who did not smoke cigarettes were of occupation levels 1 and 2; 69% and 63%, respectively, were of the occupation levels 3 and 4; 5% and 5%, respectively, were of occupation level 5; and 2% and 3%, respectively, were agricultural workers. It is of interest that the proportion of men in occupation level 5 was the same for cigarette smokers as for men who did not smoke cigarettes. Considering this in light of the mortality data given by Moriyama and Guralnick,[4] it is apparent that the slight difference in distribution by occupation levels between cigarette smokers and men who never smoked cigarettes had only a trivial effect on relative death rates of these two groups of subjects.

Check for Possible Researcher Bias

As previously described, the time trend in death rates indicates that the volunteers did a good job of screening out seriously ill men as instructed. If there was any bias in this respect between the selection of smokers and the selection of nonsmokers, it appears that the proportion of ill men screened out may have been slightly higher for heavy cigarette smokers than for men who never smoked. This is suggested by the fact that the mortality ratio for heavy cigarette smokers, compared with men who never smoked, was somewhat higher in the last two years of the study than in the earlier period (table 9).

Nevertheless, it is conceivable that, contrary to instructions, some few researchers deliberately selected men with lung cancer or other fatal diseases. If any researchers actually did select as many as five or more such sick men, it is probable that at least one of them died within the next two years. (If this were not so, bias of the sort under consideration could have little or no influence on the results of a study of this type.) Conversely, if a researcher selected five or more men and none of them died within two years, it is an indication that she probably excluded men with lung cancer and other fatal diseases.

As a check, we made a special analysis including only researchers and subjects who met the following qualifications: 1. The researcher enrolled and traced not less than 7 nor more than 20 men. 2. At least five of these men had a history of regular cigarette smoking and at least two never smoked cigarettes regularly. 3. Not a single death occurred among these men during the period of January, 1952, through April, 1954. We found that 5,445 researchers met these requirements with 55,265 men, 35,047 of whom had a history of regular cigarette smoking and 20,218 of whom never smoked cigarettes regularly. As was true of the study as a whole, the cigarette smokers in the sample were younger, on the average, than the men who never smoked cigarettes regularly. During the ensuing 18 months from May, 1954, through October, 1955, 1,056 deaths occurred among the cigarette smokers and 495 deaths occurred among the men who never smoked cigarettes regularly. Only 710 deaths would have occurred among the cigarette smokers had their age-specific death rates been the same as for men who never smoked cigarettes regularly. The

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mortality ratio between these two groups was therefore 1,056÷710, or 1.49. As compared with this, in the entire study 7,316 deaths occurred among men with a history of regular cigarette smoking, whereas 5,005 would have occurred had their age-specific death rates been the same as for men who never smoked cigarettes regularly. The mortality ratio was 1.46. The difference between these two mortality ratios (i. e., 1.49 and 1.46) is not statistically significant. We concluded that the researchers, as a group, were not biased.

Changes in Smoking Habits

Incidental to the independent tracing of subjects by mail (as previously described), we obtained information on the current cigarette smoking habits as of the period of November, 1955, to January, 1956. In addition to the subjects we wished to trace by mail, we sent questionnaires to representative samples of 600 to 1,500 subjects in each of the other smoking categories. The question on current amount of cigarette smoking was identical to the corresponding question asked in 1952. The additional groups were followed through three mailings, and about 76% replied.

Table 11 shows current cigarette smoking habits reported in 1955-1956 compared with the habits of the same men as recorded on the smoking questionnaires collected in 1952. Of the men who said that they had never smoked up to 1952, less than 1% said that they were smoking cigarettes regularly when questioned in 1955-1956. Similarly, of the men who smoked pipes or cigars regularly or who had smoked cigarettes occasionally in the past but were not smoking cigarettes in 1952, only 2.3% reported regular cigarette smoking in 1955-1956. On the other hand, of men who were smoking cigarettes occasionally in 1952 and had never smoked cigarettes regularly up to that time, 17.3% reported regular cigarette smoking in 1955-1956.

Those found in 1952 who had regularly smoked cigarettes but who stopped smoking form a particularly interesting group. Only 7.2% of those who had entirely stopped smoking by 1952 had resumed regular cigarette smoking in 1955-1956. However, on further analysis it was found that 34.9% of those who had stopped smoking for less than one year were again smoking regularly and 9.3% were smoking a pack or more of cigarettes a day in 1955-1956. In contrast, only 7.7% of those who had stopped smoking for one to five years and 2.1% of those who had stopped smoking for five years or longer resumed regular cigarette smoking. About one-quarter of those who cut down to occasional smoking took up regular cigarette smoking again.

Over three-quarters of the men who smoked cigarettes regularly in 1952 were still smoking cigarettes at the same level or at an adjacent level in 1955-1956. However, many of them had given up regular cigarette smoking. The proportion of men giving up the habit was much greater among the light smokers (36%) than among the heavy smokers (14%). On the other hand, a fairly large proportion of those who formerly were heavy cigarette smokers reported smoking lower daily amounts.

TABLE 11.—*Cigarette-Smoking Habits Reported in Period November, 1955, Through January, 1956, Compared with Habits Reported by Same Subjects in 1952*

	1952 Report								
		Smoked, but Never Cigarettes Regularly		Smoked Cigarettes and Stopped					
1955-1956 Report	Never Smoked	None	Occasional	None	Occasional	<½ Pack	½-1 Pack	1-2 Packs	2+ Packs
None, %	97.4	93.6	48.4	89.1	43.2	21.9	18.5	12.4	13.2
Occasional, %	1.7	4.1	34.3	3.7	30.4	14.3	3.1	1.3	1.0
<½ pack, %	0.3	0.6	12.4	2.1	13.2	39.5	8.9	2.3	1.2
½-1 pack %	0.4	1.0	3.5	3.3	9.7	19.2	49.9	25.6	7.2
1-2 packs, %	0.2	0.7	1.4	1.7	3.1	4.7	17.8	51.5	35.2
2+ packs, %	0.1	0	0	0.1	0.4	0.4	1.8	6.9	42.2
Total, %	100	100	100	100	100	100	100	100	100
Subtotals									
None or occasional, %	99.1	97.7	82.7	92.8	73.6	36.2	21.6	13.7	14.2
Regular, %	0.9	2.3	17.3	7.2	26.4	63.8	78.4	86.3	85.8

Age had little influence on changes in smoking habits, except among smokers of two packs or more a day of cigarettes. In this group, the percentage of those giving up the habit was greatest in the older age groups.

As previously noted, men currently smoking both cigarettes and cigars in 1952 had lower death rates than men who smoked only cigarettes. The requestioning of the subjects gives a clue as to a possible reason for this. Among men currently smoking one-half pack or more in 1952, the percentage of those reporting no regular cigarette smoking in 1955-1956 was about twice as high for men who had been smoking both cigars and cigarettes as for men who had been smoking only cigarettes. For example, among the two packs or more a day cigarette smokers in 1952, 28% of those also smoking cigars regularly in 1952 reported no regular cigarette smoking in 1955-1956, as compared with 13% of men with a history of regular cigarette smoking only.

Of those who were still smoking cigarettes regularly in 1955-1956, 28% said that they used filter-tip cigarettes. The proportion using filter-tip cigarettes was 29% among those who smoked under one pack a day and 25% among those who smoked one pack or more a day.

The changes in smoking habits of our subjects may not have been typical of what occurred among men of the same age in the United States as a whole. Some might have been influenced to change their smoking habits by the publication of our first report in 1954.

Summary

Between Jan. 1 and May 31, 1952, information was obtained on the smoking habits of 187,783 white men between the ages of 50 and 69. These were then traced through October 31, 1955. A total of 11,870 deaths were reported during that period of time. The total experience covered 667,753 man-years.

Age being taken into consideration, the death rate of men with a history of regular cigarette smoking only was found to be 68% higher than that of a comparable group of men who never smoked. The death rate of cigarette smokers increased with the amount of cigarette smoking. Among men with a history of regular cigarette smoking only, the death rate of those smoking two or more packs of cigarettes a day in 1952 was 123% higher than that of men who never smoked. Also, the death rate of men with a history of regular cigar smoking only was 22% higher than that of men who never smoked, and the death rate of men with a history of regular pipe smoking only was 12% higher than that of men who never smoked.

The death rate of men who had smoked only occasionally was not significantly different from the death rate of men who never smoked, and the death rate of men who had given up cigarette smoking for a year or more before being enrolled in the study was lower than that of men who were smoking cigarettes regularly at that time.

The findings in the last two years of the study fully confirmed the findings which had previously been reported for the earlier part of the study. Many checks were made to determine the reliability of these findings, and no errors or biases were found that could have a serious effect on them.

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This study was made possible by the cooperation of the subjects, volunteer workers, state health departments, many physicians, and personnel of divisions of the American Cancer Society. Lawrence Garfinkel, M.A., Constance L. Percy, M.S., Leonard Craig, M.A., and Herbert Seidman, M.B.A., assisted in this study.

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THYROID HORMONE.—When one reviews the facts that are currently known concerning the changes produced in the circulation of the human being by hyperthyroidism and hypothyroidism, one reaches a somewhat surprising hypothesis. Triggered by change in body temperature, produced by the increase or decrease in metabolism, the homeostatic neurocirculatory mechanism provides for change of blood flow to the skin by vasodilation or constriction. From the ensuing change in peripheral resistance, cardiac output is reflexly increased or diminished, with tachycardia and/or increase in stroke output, or the opposite, while mean arterial blood pressure is preserved in its normal range. The fact that the myocardium shares in the general metabolic effect of the thyroid hormone contributes no doubt to the maintenance of the new level of circulatory performance. Various viscera appear to function at different metabolic levels. Their varying oxygen needs seem to be satisfied in some cases by increased blood flow and in others by increased oxygen withdrawal from a more or less constant blood supply. Different organs and tissues respond to excess of thyroid hormone with various levels of metabolic rate. This probably reflects similar degrees of varying utilization of the hormone under normal conditions. Confronted by the difficulties of adapting to imbalance of this particular hormone, the circulatory system reacts in ways that are in some cases beneficial and in others detrimental.—H. M. Thomas Jr., M.D., Effect of Thyroid Hormone on Circulation, *A. M. A. Archives of Internal Medicine*, February, 1957.

CLINICAL NOTES

CONTACT DERMATITIS DUE TO "THERMOFAX" COPY PAPER

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With the constantly increasing technological knowledge, we are almost daily presented with new materials and processes to facilitate all mechanical tasks. In this present era it is not unusual to find that plastic materials are used to replace wood products, leather, or cardboard, while fiberglass frequently does duty for steel and all rubber is not necessarily obtained from trees.

The efficency required by contemporary industry has resulted in the introduction of the typewriter (which has an "inked" ribbon), carbon paper, and stencil papers (with which inks and correcting fluids are used), as well as the recently developed various types of photographic duplicating processes.

In view of the fairly frequent use of these new materials and processes, the dermatologist must constantly be aware of the possibility that these agents may be a causative factor in contact dermatitis. We have observed two patients who developed contact dermatitis from paper used in one of the newer photographic duplicating processes.

Report of Cases

Case 1.—A 63-year-old man who did office work first developed an infection of the ear for which he was given two injections of penicillin. One week later, he developed pruritus of the face and the eyelids and his jaws became swollen. A short time later he developed pruritus and erythema of the palmar surfaces of the hands, which subsequently spread to involve the dorsum of the hands and wrists.

Because of the severity of the dermatitis, he was admitted to the hospital where patch testing with a 5% solution of nickel nitrate disclosed a positive reaction. Ten days after leaving the hospital, he developed a recurrence of the dermatitis. He then recalled that he had used a "Thermofax" duplicating paper for several weeks prior to the development of the first cutaneous lesions.

Patch testing was then done with this copy paper in both its preprocessing and postprocessing state. These tests elicited markedly positive reactions. A patch test with a special hypoallergic Thermofax paper was also positive. However, tests with four types of plastic material, potassium dichromate, hat-band material, basic chromium sulfate, bichloride of mercury, copper sulfate, cobalt nitrate, and "Remington-Rand Transcopy" paper all failed to show reactions.

Case 2.—A 50-year-old man who was an office clerk first developed pruritus and erythema of the left side of the forehead, which spread rapidly to involve the greater portion of the face. Three weeks later, pruritus and exudation occurred on the dorsal surfaces and webs of the fingers of both hands. This dermatitis regressed and recurred during the following four months.

This patient had been using Thermofax machine paper for two or three months prior to the development of the dermatitis. Patch testing with the various types of Thermofax paper showed a positive reaction.

Comment

The Thermofax process involves the use of a particular type of paper which is simultaneously subjected to heat, light, and pressure while in close contact with the page which is being duplicated. After exposure of a few seconds, a direct positive image is obtained and the copy may be used immediately. This process is now coming into wide use because of its speed as well as its economy.

Although we were able to obtain samples of the copy paper from the manufacturer, no information concerning the chemical composition of this product was available. This particular material cannot, however, be considered to be a primary chemical irritant, since patients with other forms of dermatitis showed negative reactions to patch testing with this particular material.

Summary

Two patients developed contact dermatitis following the use of Thermofax copy paper. Patients with other forms of dermatitis failed to show a reaction when patch testing was done with this product.

Addendum

Since the submission of this paper for publication Dr. F. Lynch in a personal communication has informed us that the allergenic material in the Thermofax paper is a tertiary butyl catechol compound.

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Two papers on this subject are being published in the March issue of the A. M. A. *Archives of Dermatology*: Dermatitis Caused by a Copying Paper, by F. J. Kendrick, and Contact Dermatitis Due to Thermofax, by A. C. Cipollaro.

SIMPLE TEST FOR DETERMINING OVULATION TIME

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It has been reported [1] that during the midportion of the menstrual cycle a decrease in the concentration of reducing substances is present in cervical secretions. This observation suggested to one of us (C. H. B.) that significant chemical alterations in cervical secretions might take place at the time of ovulation. The variation in reducing substances might then result from a hydrolytic splitting of cervical mucus or glycogen, and glucose might be present in cervical secretions as a result of this hydrolysis. The presence of glucose could then be determined by the use of Tes-Tape.

The basis for the use of Tes-Tape as a test for glucose is the observation of Keston [2] on the simultaneous use of two enzyme systems for the detection of glucose. Glucose oxidase is a specific enzyme that catalyzes the oxidation of glucose and oxygen into gluconic acid and hydrogen peroxide. Hydrogen peroxide and orthotolidine in the presence of peroxidase then forms a blue color of varying intensity depending upon the original concentration of glucose in the specimen.[3]

Preliminary Studies

Daily tests were performed on cervical secretions obtained from normal patients to determine the presence or absence of glucose. This was accomplished by placing a strip of Tes-Tape in the cervical canal and observing if for the presence or absence of a color change. It was found that beginning approximately two days prior to the theoretical day of ovulation, a faint color change occurred on the Tes-Tape strip. This color change became of maximal intensity on the theoretical day of ovulation and then faded and disappeared within two to three days. In order to rule out the possibility of some substance other than glucose giving the positive reaction, special Tes-Tape applicators without glucose oxidase were employed in parallel tests. The results with these special applicators remained negative at the time of ovulation, while regular Tes-Tape gave a positive reaction. Thus, it would appear that it is indeed glucose that is present in cervical secretions at the time of ovulation.

Further studies have been made in an attempt to demonstrate evidence of ovulation at the time of the Tes-Tape color change. All private patients admitted to the hospital for elective hysterectomy have received the cervical glucose test on the day prior to surgery. We have observed 10 positive reactions in this group of patients. At surgery on the following day, each of the 10 patients was found to have a fresh or recent hemorrhagic corpus luteum. The significance of this observation is great, since most of these positive reactions were in women 46 to 53 years of age.

We have recently noted that follicular fluid gives a positive test with Tes-Tape. Beginning on about the 11th day of the cycle, a faint positive reaction has been demonstrated. This reaction becomes more pronounced as the cycle progresses, being deepest from the 15th to the 24th day of the cycle. We have not yet determined whether the glucose present in follicular fluid plays any part in the cervical glucose reaction.

Since it was demonstrated that a sharp rise in the concentration of cervical glucose occurred on the theoretical day of ovulation, it logically followed that the phenomenon might be employed to determine ovulation time in patients in whom artificial insemination was to be performed. A test was devised which has given a high percentage of success.

Method

Ten days after the first day of the patient's last menstrual period, the cervix is visualized with the aid of a vaginal speculum. With use of tissue forceps, a strip of Tes-Tape is inserted approximately 1 cm. into the cervical canal. The Tes-Tape strip is removed from the cervical canal after 30 seconds, placed on a clean dry glass surface, and observed for a change in color. The test procedure is repeated daily until a deep color change in noted, at which time artificial insemination is performed.

It will be seen that approximately two days prior to the day of ovulation a pale green color will develop on the Tes-Tape strip. This pale color usually appears from 3 to 30 minutes after the Tes-Tape strip has been withdrawn from the cervical canal. It should not be confused with the deep green color which appears on the day of ovulation. This color change develops promptly, usually beginning while the test paper is still in the cervical canal or while it is being withdrawn, and reaches its deepest color within five minutes. The color corresponds approximately to the 0.25% reading on the Tes-Tape color chart.

Recently, specially prepared glucose reagent applicator sticks have been used to perform the test. The applicator is tipped with cotton which has been impregnated with the Tes-Tape reagents. The color development with the applicator is very similar to that of commercial Tes-Tape.

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Results

Twenty-seven consecutive patients (all candidates for artificial insemination) were studied for ovulation time by this method. Twenty subjects became pregnant after the first artificial insemination procedure performed on the day of the deepest Tes-Tape color change. Conception occurred in three of the seven remaining patients on subsequent attempts with use of the cervical glucose test as a guide in determining ovulation time.

Summary

It is feasible to determine the day of ovulation by the detection of an increased concentration of cervical glucose. In normal patients, maximum cervical glucose concentrations occur on the theoretical day of ovulation. Furthermore, fresh hemorrhagic corpus lutea have been observed in all patients coming to surgery who have had positive cervical glucose tests on the day prior to surgery. A test making use of the presence of an increased concentration of cervical glucose at the time of ovulation has been devised. Over 70% of the patients artificially inseminated on the day of the deepest Tes-Tape color change became pregnant. The test procedure offers a simple, economical, and accurate method for the determination of approximate ovulation time.

Addendum

Recently the method of making the test has been slightly modified. Application sticks of plastic material with a cotton tip impregnated with the enzyme are now being used. These sticks are placed in the cervical canal for five minutes, and the color changes are noted as previously mentioned with the Tes-Tape.

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Material used in this study was supplied by Eli Lilly & Company, Indianapolis.

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ULTRAMICROANALYTIC METHODS NOW ADAPTABLE TO HOSPITAL USE

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Ultramicroanalytic methods for hospital biochemistry laboratories have reached the stage where they are practical for routine use and can become an integral part of most chemistry divisions.[1] Rapid progress toward simplification of techniques and apparatus has taken place in the past five years. In the chemistry department at Harper Hospital, which performs approximately 65,000 tests a year, up to 20% of the tests in a given month have been done by ultramicroanalytic techniques.

The methods of ultramicroanalysis used are, basically, standard procedures of macroanalysis which have been adapted to specially designed small-scale equipment. Naturally, some modifications are required, and it is important to avoid confusion by using ultramicroanalytic tests which will give normal value ranges comparable to the macroanalytic value ranges in a given hospital. Once a test has been properly set up and controlled, remarkably accurate results can be obtained well within acceptable clinical limits of error.

The key to successful clinical adaptation of ultramicroanalytic methods is the constriction pipet, such as the KMP or Lang-Levy type of pipet. In this type of pipet a narrowing of the lumen provides an automatic stopping point for serum and insures a high degree of accuracy. Precalibrated pipets are now available from commercial sources and greatly facilitate the installation of ultramicroanalytic methods. Other varieties, such as overflow pipets and syringe-attached straight pipets of the Kirk

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type have been used extensively in research but in our experience, at least, have not proved as practical for hospital biochemistry work.

In the general hospital laboratory, ultramicroanalytic procedures fall into four general groups, including those performed by (1) titration methods (chloride and calcium), (2) spectrophotometry (phosphate, blood urea nitrogen, glucose, total cholesterol, acid and alkaline phosphatase, bilirubin, icterus index, proteins, sulfonamides, and salicylates), (3) flame photometry (sodium and potassium), and (4) gasometer (carbon dioxide combining power or content and oxygen). Other optional methods available on the ultramicroanalytic scale include cephalin flocculation determination and electrochromatography of serum proteins. These tests comprise a most valuable collection of hospital biochemistry procedures, and the average test requires only 0.01-0.5 ml. of serum.

Much credit is due such pioneers as Natelson,[2] Caraway,[3] and Kirk [4] who have shown the way toward making practical use of ultramicroanalytic methods. From them, too, certain basic principles have evolved which are most valuable in applying macroanalytic methods to ultramicroanalytic use. For example, separation is done by centrifugation rather than by filtration. Blood is collected in capillary tubes about 10 cm. in length and 0.4 cm. in outside diameter; this blood is allowed to clot and is centrifuged, and tests are run exclusively on serum. Reagents are added directly to serum when possible. Rather than attempting to dilute solutions to a given volume, dilutions are made by adding known volumes with a pipet calibrated to contain.

In the Harper Hospital we have found it valuable to run concomitant studies on venous blood and capillary blood drawn at the same time and on quantities required for both macroanalysis and ultramicroanalysis of the same venous specimens. Of course, blanks and known standards should be included with each series of analyses.

Special equipment needed for these procedures in the laboratory includes the constriction-type pipets, an ultramicroburet (Gilmont), a high-speed microcentrifuge, flame photometer, microgasometer, and other small-sized glassware. A Beckman DU or B spectrophotometer with microcells is needed. Exclusive of the spectrophotometer and flame photometer, the cost of equipping a complete laboratory should be about $1,200. Because the equipment utilized is so small, ultramicroanalytic procedures require a minimum of laboratory space. About 13 to 16 ft. of counter space, with a sink, is adequate for the entire laboratory. Reagents are used in small quantities and may be dispensed from circular revolving reagent shelves as a further space-saving device.

A registered medical technologist should have little difficulty in mastering ultramicroanalytic techniques because, for the most part, they are merely adaptations of widely used macroanalytic procedures. The apparatus used is now widely available from commercial sources, and a knowledge of glass blowing is no longer a prerequisite for the technologist. Detailed instructions for all of the procedures can now be found in the literature.[5]

Once established, ultramicroanalytic procedures prove most valuable in pediatrics, in treatment of burns and obesity, and in control of patients on intravenous therapy. They are useful in the study of cerebrospinal fluid [6] and are helpful in checking questionable results obtained by macroanalytic methods when only small quantities of serum are available. They are adaptable to research on small animals and should open up many new opportunities for studies in this field. Concomitant use of microhematocrits and microserologic methods allows the hospital laboratory to offer a well-balanced microanalytic service to the clinician.

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CONFERENCE ON STAPHYLOCOCCIC INFECTIONS

STAPHYLOCOCCIC INFECTIONS IN THE HOSPITAL AND COMMUNITY

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Septic complications due to infection with staphylococci are currently bedeviling the professional staffs and administrators of hospitals. Concordant reports to this effect are becoming available from all medically advanced parts of the world.

The Conference on Staphylococcic Infections in the Hospital and Community was convened in Cleveland on Nov. 14, 1957, under the authorization of the trustees of the American Medical Association. The American Academy of Pediatrics; the American College of Obstetrics and Gynecology; the American College of Surgeons; the American Hospital Association; the American Nurses' Association; the American Society of Clinical Pathologists; the California Department of Public Health; the Communicable Disease Center of the U. S. Public Health Service; the Food and Drug Administration; the Hospital for Joint Diseases, New York; Jefferson Medical College, Philadelphia; Office of the Surgeon General, U. S. Public Health Service; the State University of Iowa; the Seattle–King County Department of Health, Washington; the University of Pennsylvania; and the Veterans Administration were represented, in addition to the American Medical Association.

The conference included four formal papers, in each instance followed by general discussion, and the papers of three invited discussants. The formal papers and two of the paper in discussion are printed in full immediately following this introduction. The conclusions of the conference are embodied in resolutions adopted without dissent by the conference and which have since been ratified by the trustees of the American Medical Association. These conclusions are as follows:

Cogent evidence has been presented of the widespread dissemination throughout the hospitals of the United States and Canada and of other countries of a strain or strains of Micrococcus [Staphylococcus] pyogenes var. aureus with very special biologic characteristics. These include high communicability from infected person or carrier to contacts, a tendency to produce nasal carriers, a tendency to produce lesions of the integument and septic complications of wounds and to invade sites of reduced resistance, and a special propensity for developing resistance to the antibiotic agents used to combat these staphylococci. In a few proved instances staphylococcic secondary pneumonia has brought a fatal termination to Asian influenza.

One epidemiologic picture which has recurred frequently is one in which the "epidemic strain" of Staphylococcus has become associated with a newborn nursery and has infected the babies therein. The babies infect the nursing mothers, causing breast abscesses. Both infected mothers and babies may then be sources of spread in families and community. Probably both asymptomatic carriers and fomites may be involved in the continuance of the infectivity of the nursery environment.

Two general contributing causes to this serious situation can be discerned: (1) A tendency to relax the rigorous aseptic precautions in hospital "housekeeping" and procedure, relying overmuch on antibiotics to suppress infections. (2) The very peculiar biologic characteristics of the epidemic strain or strains, including their special propensity for becoming resistant to an increasingly wide range of antibiotics and chemotherapeutic agents.

Well-documented instances are on record in which vigorous investigations of the situation in a given hospital and rigorous application of all available measures of control and eradication have essentially controlled the situation in the hospital in question for the time being.

However, it is an easily documented fact that basic information about the ecology, pathogenesis, immune relationships, and mutability of staphylococci has lagged far behind basic information concerning other pyogenic pathogens such as the pneumococci and streptococci. The staphylococci are, for instance, less readily amenable to the well-known defensive action of leukocytes, as well as to the action of chemotherapeutic and antibiotic agents.

The participants of the conference strongly made the following recommendations:

"(1) That every hospital establish a responsible officer or committee charged with the investigation and control of infections within that hospital and with the institution of procedures and practices designed to prevent such infections.

"(2) That encouragement and funds be channeled into scientific research concerning the ecology and epidemiology, and the immune relationships of pyogenic staphylococci, their relationships to the defensive cells of the body and the mechanism of their mutability to drug and antibiotic resistance."

In view of the statement and agreement with the recommendations outlined above, the participants approved the following resolutions:

"(1) The Conference is impressed by the seriousness of infections arising in hospitals.

"(2) It believes that there should be diligent research as to the causative organisms, and as to the special properties which render them so infective and dangerous, and for the search of immunologic and chemotherapeutic measures against them.

"(3) In the meantime, the Conference believes that it would be useful and constructive if the A. M. A. were to recommend to every hospital that it establish in its staff a special standing 'Interdepartmental Committee on Infections,' headed by

Chairman, Committee on Research, Council on Drugs, American Medical Association.

Summary of the Conference on Staphylococcic Infections, sponsored by the American Medical Association, Cleveland, Nov. 14, 1957.

an especially qualified person, for the establishment and enforcement of adequate directions for asepsis and isolation in the hospital.

"(4) There is need also of community participation in these problems, as, for instance, by the County Medical Societies, local health departments, and by an Interhospital Committee on Infections."

The wide-ranging discussions of the conference are for the most part covered in detail in the papers appearing in this issue of THE JOURNAL. An exception is that of Dr. Reimert T. Ravenholt, who presented a splendid historical survey and analysis of current problems of staphylococcic infection in hospitals and communities under the title of "The Hospital Environment and Staphylococcal Disease." Dr. Ravenholt's lecture introduced a panel discussion on epidemiologic aspects of staphylococcic infections, presented before several sections of the American Public Health Association, which occupied the morning preceding the conference under the Committee on Research. Dr. Ravenholt's lecture will appear in the March, 1958, issue of the *American Journal of Public Health*.

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PRINCIPLES OF MANAGEMENT OF STAPHYLOCOCCIC INFECTIONS

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The results of antimicrobial therapy in patients with staphylococcic infections are difficult to evaluate for numerous reasons. These infections vary in severity from small pustules on the skin to overwhelming sepsis with bacteremia and formation of distant abscesses. Many patients having furunculosis frequently improve spontaneously or after surgical incision with adequate drainage. The addition of other therapeutic agents may prevent the spread of infection and accelerate the healing process, but these effects are often difficult to demonstrate. Similarly, therapy is difficult to evaluate in patients with bacteremia and septic complications, which may include abscesses of almost any organ in the body. When endocarditis is present, it is frequently complicated by erosion and rupture of the valve with sudden myocardial failure and death; and the incidence of fatality in these patients is high with any therapy. Active and passive immunization by the use of vaccines, toxoids, and antitoxins has not proved promising to date.

More antibiotics have been produced as additional therapeutic agents for staphylococcic infections than for any other infectious disease. The discovery and production of new and effective antibiotics will be necessary in the future, but their effectiveness will be limited by the same factors which restrict the action of the currently employed antibiotics. Successful management of staphylococcic disease may therefore depend on the developmental stage of the abscess, the localization of the infection in areas that are accessible to surgical intervention, and the institution of therapy with effective antimicrobial agents early in the course of the illness.[1]

The principles of therapy of staphylococcic infections can be formulated on the basis of previous experience, a knowledge of the factors which involve the patient, the etiological agent, the pathological process, and the medical and surgical forms of therapy. Some of these factors which are listed in the table should be emphasized if one is to improve the methods of control and cure of staphylococcic infections.

Factors of the Etiological Agent Which Affect Therapy

Strains of staphylococci vary in degree of virulence and the biological characteristics of the organisms which relate to their virulence are not well understood. The use of present laboratory methods reveals no differences in virulence between known pyogenic strains and the coagulase-positive cultures from human carriers [2]; however, there is clinical evidence that strains which are dispersed from infections are more virulent than those of the same bacteriophage types carried in the noses of healthy carriers.[3]

There is convincing evidence that these microorganisms are spread to clothing, bed linens, air, dust, and other fomites in the environments of patients with discharging abscesses or wounds.[4] When such ubiquitous bacteria are resistant to several antibiotics, the problem of management of infected patients attains serious magnitude. Therefore, it is

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of utmost importance to maintain rigid aseptic techniques, particularly in hospitals, in an attempt to prevent the occurrence of staphylococcic infections in patients.

Staphylococci are notorious for their ability to develop resistance to antibiotics. This brings about the selection and propagation of antibiotic-resistant strains in hospitals where antibiotics are intensively used in therapy. Staphylococci of various types are widely distributed and are present in the anterior nares of approximately 80% of hospital personnel, with coagulase-positive strains present in about 50%. Approximately 12% of people working in hospitals carry the strains that cause the majority of hospital-acquired staphylococcic infections.[5] The incidence of such hospital-acquired infections is reduced when methods for the control of the carrier state are attained, thus preventing spread from human carriers to susceptible hosts.[6]

The wide environmental distribution of staphylococci and their presence on the skin accounts for the contamination of specimens prior to submission to the bacteriological laboratory. Extreme precautions must therefore be taken in collecting and handling specimens for bacteriological study. When obtaining blood for cultures, a wide area of the skin should be thoroughly cleansed with soap and water and dried with alcohol. This same area is then painted with tincture of iodine, which can be removed with Richardson's solution after the specimen is obtained.

The presence of staphylococci in blood cultures must be evaluated to discover whether the organisms represent contamination or the actual pathogen. As this can be a very difficult decision, information may be gained from the coagulase test, since the strain coagulating plasma is probably pathogenic. The coagulase test, however, does not resolve the situation entirely for coagulase-positive contaminants may occur.

The collection of bacteriological specimens from chronic ulcers or draining sinus tracts should not be attempted at the time of first examination. These sites are frequently contaminated with gram-negative bacilli, particularly Proteus and Pseudomonas species,[7] as well as other strains of staphylococci. The infected area should be cleansed and drainage encouraged for 12 to 24 hours in order to eliminate these secondary contaminating bacteria. During drainage the area should be covered with sterile, moist compresses of isotonic sodium chloride solution. Specimens of purulent material should then be collected with a sterile applicator or glass pipet. This technique will aid in the isolation of the specific agent and will eliminate, to a great extent, contaminating bacteria which have no role in the infectious process. Adherence to these procedures may prevent ineffective, expensive antibiotic therapy and will contribute to the proper evaluation and treatment of the patient's disease.

Factors of the Host Which Affect Therapy

The determinant factors of host susceptibility are unknown, and the physiology of the host which affects therapy is poorly understood. In the therapy of cutaneous staphylococcic infections, attempts should be made to cleanse the surface area and maintain excellent hygiene of the skin and mucous membranes. Patients with recurrent furunculosis should not cleanse with soap and immersion baths but rather with soap and shower baths, which are more effective in the removal of pathogenic bacteria from the skin. The area of skin surrounding a draining abscess should be cleansed frequently with 70% alcohol.

A topically applied antibiotic ointment may decrease the chances of entry of micro-organisms into new sites. A covering of gauze should be applied,

Factors Which Affect Therapy in Staphylococcic Infections

- **Etiological Agent**
  - Virulence
  - Susceptibility to antibiotics
  - Appearance of mutant strains
  - Ubiquity
    - Reservoir—nose and intestines
    - Survival in environment
- **Patient**
  - Hygiene
  - Nutrition
  - Existence of other diseases or abnormalities
    - Diabetes mellitus
    - Vascular insufficiency
    - Cardiovascular defects
    - Hematological defects
    - Predisposing infections
    - Foreign bodies
    - Open wounds, burns
    - Unknown constitutional factors
- **Infection**
  - Cellulitis—early
    - Increased vascularity
    - Diffusion of antimicrobial agents
  - Abscess—late
    - Central core of necrotic tissue
    - Fibrous inflammatory wall
    - Thrombosis of blood vessels
    - Decreased vascularity
    - Decreased diffusion of antimicrobial agents
    - Protection from antimicrobial agents by intracellular location of bacteria

but the use of adhesive tape should be avoided, since its removal is traumatic and opens new portals of entry of infection into the skin.

The clothing and bed linens used by an infected person become heavily contaminated and should be changed frequently. These should be laundered by a method that removes or destroys the pathogenic bacteria. Plastic or rubber covers will decrease the contamination of mattresses and pillows and should be disinfected daily. The benefit obtained from the removal of the staphylococci from the nose of infected patients has not been demonstrated, but is the subject of further study.

A careful search should be made for concurrent disease or abnormality, for staphylococcic infections are frequently secondary to other pathological states. Some examples include diabetes mellitus, vascular insufficiency, and congenital or acquired cardiac de-

fects. Patients with hematological abnormalities such as neutropenia, agranulocytosis secondary to medications, leukemia, or other malignant diseases are susceptible to intercurrent staphylococcic infections. Influenza, tuberculosis, bronchiectasis, and other abnormalities may be predisposing factors for the development of staphylococcic pneumonia, pulmonary abscess, and empyema. Surgical sutures, soil, wooden splinters, and other foreign bodies serve to retard the defensive mechanisms against bacterial invasion.[3] Open surgical wounds are known to become contaminated with staphylococci even in well-managed operating suites.[4] There are other unknown constitutional factors which affect host susceptibility which must be investigated before we understand the frequent spontaneous appearance of staphylococcic infections in otherwise healthy individuals.

Factors of the Pathological Process Which Affect Therapy

It is particularly advantageous in the management of staphylococcic infections to understand the pathogenesis of the disease process. Knowledge of the changes that occur in the infectious process and the proper application of medical and surgical therapy may make the difference between therapeutic success and failure in the potentially seriously ill patient. Early in the process of staphylococcic invasion of tissue there is cellulitis and an increased vascularity of the area. During this period the use of antibiotics in conjunction with warm, moist compresses may be of value and result in the subsidence of the infection. Such remission is often observed in patients with mastitis and cellulitis, if antimicrobial therapy is instituted early. The later formation of an abscess with its central core of necrotic tissue interferes with the action of therapeutic agents. The blood vessels become thrombosed and vascularity is thus diminished, with consequent decrease in the concentration of antibiotic agents in the center of the abscess. The surrounding fibromembranous inflammatory wall interferes with the diffusion of antibiotics into the infected site. Surgical incision of the abscess with evacuation is of maximum benefit during this phase of infection.

Antibiotics in Therapy of Staphylococcic Infections

It is apparent that in medical centers an increasing number of infections are produced by staphylococci which are resistant to penicillin, streptomycin, and the tetracyclines. Fortunately new antibiotics have been produced which are effective against these micro-organisms. However, in hospitals where therapeutic agents such as these are used, strains of Staphylococcus are encountered which are resistant to chloramphenicol, erythromycin, and novobiocin. To make maximum use of antibiotics in serious infections, the physician should know the degree of antibiotic resistance or susceptibility of the invading strain. To obtain this information requires 24 to 48 hours after the bacteriological specimen is submitted to the laboratory. Consequently, immediate therapy must be empirical and based on the probability of certain antibiotics being effective. If the physician is aware of the characteristics of "hospital" or "epidemic" staphylococci, which usually number from three to six different strains, the correctness of his empirical judgment will probably be confirmed by the results of the laboratory tests of antibiotic susceptibility. When the physician is familiar with this problem there is usually no reason for changing the therapeutic program after the completion of bacteriological studies; consequently, the patient has an advantage of two to three days of maximum therapeutic efficacy.

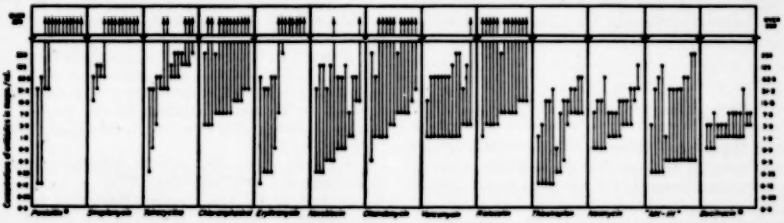
Study of Relative Effectiveness.—The following investigations of the bacteriostatic and bactericidal activities of 13 antibiotics were made in an attempt to compare the relative effectiveness of the antibiotics against staphylococci. Cultures from 13 hospitalized patients with staphylococcic infections were collected. The cultures represented five different bacteriophage types which were known to cause most of the hospital-acquired infections at the Jefferson Medical College Hospital of Philadelphia during 1957. Seven of the cultures were of bacteriophage type 52/42B/81/44A (designated type 80/81 by The International Typing Reference Center; see article by Blair and Carr in this issue, page 1192), which is reported to be the major cause of staphylococcic infections in the hospitals in many parts of the world. The other strains which were studied included three cultures of bacteriophage type 44A and one culture each of 52A/79, 3A/3B/3C/53, and 44A/81.

Method: The tube dilution method,[5] employing serial twofold dilutions of antibiotics, was used. The bacterial inoculum consisted of 0.5 ml. of a 1:100 dilution of an 18-hour broth culture. The minimum inhibitory concentration (bacteriostatic concentration) of each of 13 antibiotics was determined for each of the 13 cultures. The antibiotics used in this study were penicillin, streptomycin, tetracycline (Achromycin, Tetracyn, Panmycin, Polycycline, Steclin), tetracycline phosphate (Tetrex, Panmycin V, Sumycin), tetracycline and sodium metaphosphate (Achromycin V), chloramphenicol (Chloromycetin), erythromycin (Erythromycin, Ilotycin, Erythrocin), novobiocin (Albamycin, Cathomycin), oleandomycin phosphate (Matromycin), vancomycin, ristocetin (Spontin), neomycin, bacitracin, Thiostrepton, and MK-111 (Streptogramin). Three of the antibiotics—vancomycin, thiostrepton and MK-111—were available only for experimental clinical investigation at the time of this study. The bacteriostatic results are recorded as the lowest points of the bars in the figure. The contents of the test tubes which showed no evidence of growth after incubation were then cultured to determine

the minimum bactericidal concentrations for each culture. The bactericidal concentrations are represented as the highest point of the bars in the figure. The length of the bars thus shows the range between the minimum bacteriostatic and bactericidal concentrations for each of the cultures. For practical purposes a culture is considered to be susceptible if its growth is inhibited by 1 mcg. of an antibiotic per milliliter of broth. It is moderately susceptible if inhibition occurs in a range of 1 to to 10 mcg. per milliliter and resistant if more than 10 mcg. of an antibiotic per milliter is required to inhibit growth. The importance of the bactericidal action of an antibiotic in therapy is not well understood, since these effects are not commonly determined and, therefore, correlations are unknown.

Findings: Only 2 of the 13 cultures were susceptible to penicillin, and all were resistant to streptomycin. Three cultures were susceptible to tetracycline in concentrations that could be therapeutically effective. The minimum bacteriostatic activity of chloramphenicol ranged from 3.0 mcg. per milliliter to 31.2 mcg. per milliliter with a lack of bactericidal effect. Approximately one-half of the cultures were inhibited by therapeutic concentrations of erythromycin, but the drug was not bactericidal for 8 of the 13 strains in the maximum concentrations that were tested. Novobiocin was inhibitory in concentrations below 3.9 mcg. per milliliter in 11 of the 13 cultures and bactericidal in a range of 7.8 to 125 mcg. per milliliter in 11 instances. Oleandomycin was bacteriostatic in concentrations of 0.5 to 31.2 mcg. per milliliter and lacked bactericidal activity for 10 of the cultures. Vancomycin was bacteriostatic for all cultures in concentrations of 1.8 to 3.9 mcg. per milliliter; was bactericidal in concentrations of 15.6 to 62.5 mcg. per milliliter for eight cultures, and lacked bactericidal effect for one culture. Ristocetin was bacteriostatic in a range of 1.8 to 15.6 mcg. per milliliter, but lacked bactericidal action for 12 of the cultures that were employed in this study. Thiostrepton was bacteriostatic in concentrations of 0.12 to 7.8 mcg. per milliliter and exerted effective bactericidal effects in a range of 0.9 to 62.5 mcg. per milliliter. Neomycin inhibited growth in a range of 0.9 to 31.2 mcg. per milliliter and was bactericidal from 7.8 to 125 mcg. per milliliter. Bacitracin was bacteriostatic in concentrations of 0.9 to 3.9 mcg. per milliliter and was bactericidal in a range of 3.9 to 31.2 mcg. per milliliter. MK-111 was bacteriostatic from 0.25 to 0.5 mcg. per milliliter and was bactericidal from 1.8 to 250 mcg. per milliliter.

These results indicate that penicillin, streptomycin, and the tetracyclines have little or no effect on these "epidemic" strains of staphylococci and would not be expected to be of therapeutic benefit. The action of erythromycin cannot always be predicted since approximately 50% of the strains at the Jefferson Medical College Hospital are resistant to this antibiotic. The staphylococci are moderately susceptible to the bacteriostatic effects of chloramphenicol, but this antibiotic lacks bactericidal effects. The new antibiotics—novobiocin, oleandomycin, and ristocetin have beneficial antimicrobial effects against these micro-organisms. It would appear from the above results that oleandomycin and ristocetin are lacking in bactericidal action on the strains used in this study and are less bacteriostatic than novobiocin. Neomycin is effective and has its greatest usefulness in topical therapy of staphylococcic infections. It can be administered parenterally as a last therapeutic resort, but deafness may result from this use. Bacitracin is also effective in vitro but intramuscular administration should be limited to a daily dose of 1,000 units per kilogram because of possible toxic effects. Vancomycin, thiostrepton, and MK-111 are antibiotics which are effective against the "antibiotic-resistant" strains of staphylococci, but since they are in the process of clinical investigation at the time of this study, and are not as yet complete, they will not be discussed in this report.



Bacteriostatic and bactericidal action of antibiotics on staphylococci. Each bar represents range of antibiotic effects on one culture. Bottom and top of bar represent bacteriostatic and bactericidal concentrations respectively. Concentrations of penicillin and bacitracin measured in units per milliliter.

A general knowledge of the antibiotic susceptibility of strains of "epidemic" staphylococci and the concentrations of antibiotics attainable in vivo with different forms of administration is of aid in the

selection of the antibiotics of choice in the treatment of patients with severe staphylococcic infections. Relative toxicity of each antibiotic should be considered in the selections. When combinations of antibiotics are employed, the etiological agent must be susceptible to each antibiotic that is used. If an abscess is inaccessible or its location is only suspected or unknown in a patient with bacteremia, the most effective antibiotic should be administered in high dosage by means that will provide maximum concentrations of the drug in the plasma and tissues. Intravenous administration may be of more beneficial use than oral or intramuscular therapy during this stage in patients with severe illness. The administration of the antibiotics should be continued for sufficient time to allow the elimination of the infectious agent. A relapse may occur if antimicrobial therapy is discontinued too early in patients with previous septicemia, even though the patient is afebrile.

Summary

The basic principles of management and therapy of staphylococcic infections have been considered. Staphylococcic infections vary from minor infections of the skin to fatal overwhelming septicemia. The formation of abscesses limits the effectiveness of antimicrobial therapy and necessitates surgical intervention. Stringent aseptic techniques should be employed in an attempt to prevent re-infection of new skin sites of patients with purulent drainage to the external surface. Aseptic methods are also important in decreasing the spread of these bacteria to healthy people who may become carriers, as well as to other susceptible patients. The comparative in vitro effectiveness of 13 antibiotics on "epidemic" strains of staphylococci have been evaluated as an aid in the selection of antimicrobial therapy.

This study was supported in part by a research grant from the National Institute of Allergy and Infectious Diseases, U. S. Public Health Service.

The vancomycin used in this study was supplied by Eli Lilly & Company, Indianapolis; the thiostrepton by E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, New York; and the MK-111 (streptogramin) by Merck, Sharp & Dohme, Division of Merck & Co., Inc., Rahway, N. J.

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HYPERCALCIURIA FOLLOWING POLIOMYELITIS.—Urinary calcium, phosphorus and creatinine excretion were studied serially after paralytic poliomyelitis in 27 adults and children for periods lasting 2 to 12 months. Less detailed observations were made on 27 additional patients. The patients had paralysis which ranged from mild cranial nerve involvement to total quadriplegia. The degree of immobilization ranged from practically none to severe. All patients studied immediately subsequent to acute illness had a significant increase in urinary calcium excretion, which reached a maximum in the second to eighth weeks after poliomyelitis. This early hypercalciuria attained levels which averaged twice the predicted normal urinary excretion for age and sex. The rise was independent of the site or degree of paralysis or immobilization. Hypercalciuria ceased by the 14th week after onset of poliomyelitis in patients with bulbar and high spinal paralysis, whereas it continued up to 12 or more months in severely paralyzed persons. Only two patients had excessive calcium excretion lasting more than 15 months after onset of poliomyelitis. Both had renal calculi. The evidence suggests that demineralization after poliomyelitis is initiated and maintained by systemic neurohumoral factors as yet only partially clarified. These factors appear at least to supplement any loss of stress and strain on bones resulting from immobilization.—M. F. Dunning, M.D., and F. Plum, M.D., Hypercalciuria Following Poliomyelitis, *A. M. A. Archives of Internal Medicine*, May, 1957.

PROGRAM FOR PREVENTION AND ERADICATION OF STAPHYLOCOCCIC INFECTIONS

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At Temple University Hospital we insist that all infections be reported promptly to the hospital administrator or some similarly central person. This obtains recognition of the true state of affairs, which is not admitted by some and not recognized by others. Adherence can be obtained from certain reluctant staff members by holding the resident responsible for reporting. Residents usually have sufficient respect for authority to adhere to the rules. The department of bacteriology is one of the best sources for reporting infections.

We appointed a committee made up of a chairman from general surgery, Dr. H. Taylor Caswell, and representatives from each surgical specialty, from pediatrics, anesthesiology, bacteriology, nursing, and medicine. They meet weekly, receive reports of infections from the administrator and the department of bacteriology, investigate each case, and make recommendations for conduct of hospital procedures, changes, etc. They are thus able to watch progress and to assess the values of various steps taken.

Fertile methods of investigation and/or correction were to (1) check on all sterilization and laundry procedures; (2) check on all personnel in attendance; (3) return to the strict aseptic techniques of the pre-antibiotics era; (4) discourage indiscriminate use of antibiotics; and (5) analyse the debatable move of routine use of antibiotics in surgical wounds.

Results of Program

Check on Sterilizing and Laundry Procedures.—Instruments, gloves, linen, and water were found innocent of infection and satisfactory on all counts.

Laundry was sterile at the end of process—the man in charge of the laundry was so confident of his processing that he drank the last rinse water while inspectors watched him. However, linen contaminated with so-called hospital Staphylococcus or any other noteworthy pathogens was given special treatment. At the source of contamination, it was placed in linen bags with red rims for identification. These were handled as separate batches in laundry by gloved workers and also ended up sterile by the laundry processing.

On the wards and private floors, patients with staphylococcic or other serious infections were placed under modified isolation technique, and their linen and blankets placed in red-rimmed cloth bags for special handling as stated above. Early in our search, it was found that blankets were not being changed or sterilized between patients. This was corrected. Oiling of blankets and linens was not adopted. Mattresses are encased in plastic covers which can be cleansed with antiseptic. Wet mopping of the entire hospital was reinstituted to diminish dust, and antiseptics were used on mops in operating rooms and spaces occupied by infected patients. Doctors used rubber gloves to handle infected patients and avoided contact of clothing, etc., with bed or trappings of infected patients. Soap and water and alcohol were used freely on the hands of attendants of all types. An effort was made to break the chain of transmission in any direction, which should include the electrodes of electrocardiograph, x-ray tables, food trays, etc. Great care was taken to avoid placing surgical patients in the same room with infected ones.

A special operating room was used only for contaminated cases and these were placed at the end of operating lists. The room itself was then mopped with antiseptic. Since many emergency operations are done for some effect of infection, they, too, were done in this special operating room. An effort was made, with varying success, to keep this room unused and aired for 24 hours after each use. The problem faced by Shooter and co-workers [1] of airborne contamination from adjacent wards, etc., due to exhaust type ventilation sucking air through the cracks of closed doors into operating rooms, as demonstrated by titanium chloride smoke and multiple culture plates, did not have to be faced, because our operating rooms were air-conditioned and under some positive pressure blowing air out of the rooms. Recirculated air passes through filters to avoid redistribution of infection.

Check on Personnel.—All medical personnel were encouraged to stay off duty if they developed infected lesions, and the doctors helped to police this phase, occasionally having to insist that someone leave his or her duty. Local lesions were treated by compresses and drainage. Only those who were definitely ill were given appropriate antibiotics. Medicated soap (hexachlorophene) was prescribed for bathing, and those with repeated infection were treated with vaccine, either autogenous or a stock vaccine of the "hospital Staphylococcus" as indicated by cultures, and by courses of novobiocin or chloramphenicol. The antibiotics were routinely

From the Temple University Medical Center.
Read before the Conference on Staphylococcic Infections, sponsored by the American Medical Association, Cleveland, Nov. 14, 1957.

effective, the vaccine questionable. Surgical wounds were treated with early adequate drainage and topical irrigations with aminoacridine, antibiotics, etc., and systemically administered chloramphenicol and novobiocin.

Nasal cultures were made on 640 members of hospital personnel and 41% were found to harbor a coagulase-positive Staphylococcus, but only 4% were of the significant phage type 42B/52/81 (designated type 80/81 by the International Typing Reference Center [see article by Blair and Carr on page 1192 of this issue]) which was responsible for 69% of the hospital infections. Serial cultures of these carriers showed considerable variation between the presence and absence of positive cultures. We arrived at the conclusion that the nose was not an important source of contamination. However, these people were warned to take special precautions but were not treated with antibiotics. Consideration was given to a universal vaccination of all personnel but there were many arguments against it, chiefly the various strains of Staphylococcus causing the lesions, and it was not instituted. Nurses' aides, orderlies, etc., were more difficult to watch but seemed to have very few infections. Student nurses seemed most vulnerable and the majority of their infections were on exposed areas suggesting contact transmission.

Return to Strict Aseptic Techniques of Pre-antibiotics Era.—For those connected with actual surgical procedures, we abandoned all the short cuts and easygoing procedures which had grown up in most hospitals in the past 10 years and reverted to the strict aseptic techniques of the pre-antibiotics era.

Our medicated (hexachlorophene) liquid soap, although sterile in its concentrated form, was found, when diluted for use, to harbor a resistant Escherichia coli, as did the dispensers. We discarded the 5-minute scrub with this for a 10-minute scrub with white bar soap and sterile brush. Between operations, five minutes sufficed if hands touched nothing after removing the gloves of the previous operation. A 70% alcohol bath for one to two minutes completed the hand preparation. Multiple check cultures proved this effective even after two to three hours of operating.

Multiple layer gauze masks were replaced by thick filter types. These and caps were changed for each operation.

Separate clean shoes for operating rooms only were required of even the students. Hypochlorite mats in large rubber "flats" were placed for wiping shoes before entering the operating suite. Even visiting physicians were required to exchange all street clothing for scrub suits and to wipe their shoes on the hypochlorite mats. This was quite a hardship for them but has been grudgingly accepted. Visits outside the operating suite to make rounds, visit laboratories, etc., in operating room clothes were discouraged. When such was deemed necessary, street shoes were worn for that trip and a clean scrub suit donned upon returning.

After anesthesia had been induced, the operative field was cleansed with bar soap and scrubbing brush, wiped off with a sterile towel and further prepared with a brisk scrub with ether sponges and generous application of tinted alcohol. Procedures on patients with furuncles or other evidence of infection were postponed unless surgery was mandatory.

Careless methods of dressing wounds were deleted. Nurses carefully schooled in sterile technique were again put in charge of dressing carriages. For infected wounds, gloves were again used as well as the usual instruments. Soiled dressings were placed in paper bags to be incinerated or autoclaved and all instruments, linen, gloves, etc., used in the procedure were placed in paper bags for sterilization before being cleaned or handled in any way. After this, they went through the usual cleansing, packing, and sterilizing.

Discouragement of Indiscriminate Use of Antibiotics.—We have tried vigorously to combat the indiscriminate use of antibiotics so often given futilely for various mild illnesses, such as the common cold, and in small amounts which tend to immunize rather than mortify bacteria, engendering resistant strains, or to destroy competitive normal flora, permitting pathogen growth. Unfortunately, patients have been taught to expect this of the "modern" doctor. Our staff is alerted to the danger and heeds the warning.

Routine Use of Antibiotics in Surgical Wounds.—Lastly, a very debatable step was taken. For one year, from March, 1956, to March, 1957, to avoid seasonal influence, most of the clean wounds were treated with 10 cc. of saline containing 10,000 units of penicillin per cubic centimeter as they were being closed. This was combined with the other measures mentioned above so that its value, if any, is difficult to assess. Certain it is, however, that an alarming increase of clean wound infections to 5% was reduced again to a tolerable rate of 0.4 to 1.0%.

For the past eight months, this antibiotic instillation has been omitted without appreciable increase of infections of clean wounds.

Thus we illustrate a logical and practical, although somewhat tedious, program which brought us back to a level of staphylococcic infection which was not so frightening. Noteworthy is the fact that there is no one source of error, but many small facets which must be corrected and vigilantly policed.

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HYGIENE AND EDUCATION WITHIN HOSPITALS TO PREVENT STAPHYLOCOCCIC INFECTIONS

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Throughout recorded history physicians have made serious efforts to prevent cross infections in hospitalized patients. Modern bacteriology supplied a reasonable rationale for the formulation of methods. The detailed measures essential to aseptic and isolation techniques became accepted by all hospital personnel as a matter of course for regular daily operations. Considerable success in preventing intrahospital infections was a result. A change in approach has begun to develop over the past 20 years, with the introduction of effective chemotherapeutic agents. Sulfapyridine, in 1938, began the modern therapeutic era for Staphylococcus (Micrococcus) pyogenes.[1] Because of the effectiveness of antimicrobials, a tendency to overlook the time-tested methods became apparent.[2] The use of antimicrobials for preventing staphylococcic infections became relatively ineffective. The facility with which strains of Staphylococcus pyogenes develop resistance to antimicrobials is a discouraging aspect of the experience with each antibiotic discovered.[3] The situation at present finds specific therapy increasingly limited in value, while the relatively successful measures for prevention by isolation are rusty from disuse, or were never learned in the first place. Today, there is ample, and often tragic, evidence that the number of hospital-acquired infections due to strains of antimicrobial-resistant staphylococci have created a major problem.

The emergence of antimicrobial-resistant strains of organisms is of significance to the future of antibiotic therapy.[4] The effectiveness of antimicrobials introduced during the past 23 years has reduced the extent of fundamental research on staphylococci. Subsequent developments, particularly the recent experience with staphylococci, suggests that a return to basic studies of immune mechanisms and host-parasite relationships is urgently needed. The possibility exists that present methods may eventually fail to control infections caused by many bacteria.[5] Several groups of bacteria have already become relatively ubiquitous.[6]

The purpose of this paper is to consider the methods available now for prevention and control of staphylococcic infections in hospitals, as they relate to the environment, including personnel. Formal and informal types of educational techniques cannot be divorced from any aspect. Sufficient information about the problem, and acceptance of personal responsibility for preventive measures by every person, are requirements to success.

The ecology and epidemiology of the subject are directly pertinent to the purpose. Reference will be made to certain aspects considered important to the rationale for the suggestions contained in this paper. A few of the many good papers published recently to summarize various features of the problem are among the references.[7] New data are rapidly accumulating. A body of knowledge has been acquired which seems to form a clearer epidemiologic pattern than heretofore. This background may help develop more effective methods to control cross infections due to staphylococci. Eradication of the intrahospital-acquired infections remains a goal the answer to which is not provided by the knowledge to date. The urgency of the problem demands that all preventive measures against staphylococcic cross infections, promising for control, should be instituted now, and improved whenever better data become available.

The literature contains different, sometimes conflicting, views expressed by different authors on the epidemiology and best methods of control of staphylococcic infection, each based on data collected. Therefore, much of the description and many of the recommendations in the sections to follow are of necessity based upon personal evaluation of published information, experience, and judgment.

Nature of the Problem

Since May, 1956, 115 hospitals in California (of approximately 400) have given official recognition to the presence of staphylococcic infections acquired in the hospital. All wards and services, including hospital personnel and attending staff, have been affected. When an outbreak occurs in any hospital, the attention is usually focused on one or more units which are involved at the time, but the hazard is present in all areas. Many patients have died from staphylococcic infections acquired in the hospital. Staphylococci cause most instances of "terminal pneumonia." In many of the fatal cases of influenza due to the recently encountered Asian strain, which have been carefully studied, patients have had a complicating or associated staphylococcic pneumonia.

The accumulated evidence suggests that nearly every hospital has experienced increased numbers of intrahospital-acquired staphylococcic infections

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that are antimicrobial-resistant, whether recognized or not. Conditions have been found to be nearly the same in all parts of the world where studies have been made.[3]

Letourneau [2] expressed his concern in a forceful manner, worthy of quoting: "There is a serious problem facing hospitals today which demands recognition. More important than relationships between medical staff and administration, more important than financing of hospitals, more important than the nursing shortage, more important than personnel management, this problem involves the life and death of our patients." This statement was made in connection with nosocomial infections in general, not limited to cross infections due to staphylococci per se, but directed essentially toward this important example. Many thoughtful physicians believe that the situation is the most immediately urgent of all in the field of infectious diseases.

The occurrence of frank outbreaks of infections has begun in many hospitals during the last two to four years. Awareness by the medical profession generally is gradually developing. Nevertheless, a near majority of hospital staff personnel remains innocent of the dangerous Staphylococcus which exists among them. Education within hospitals should be concerned with demonstrating this truth.

Estimation of Prevalence.—A means of estimating the extent to which intrahospital-acquired infections are occurring is important to understanding the nature of the problem. Rarely, if ever, has this been defined with any degree of exactness. Comprehensive studies of localized units or hospitals are available, but do not provide other than an estimate of prevalence.

Obvious reasons explain the difficulty in obtaining accurate figures. An organized system for gathering data is lacking. Man has lived with staphylococci as long as he can remember. Staphylococci cause the most minor, the most terrible, and the most frequent bacterial infections. It would seem that familiarity bred of propinquity has caused neglect of sufficient study of this group of organisms. Classification and clinical recognition require clarification. The profession has considered staphylococcic cross infections to be evidence of "bad luck" or laxity in preventive measures. In California, prior to May, 1956, the diagnosis of a staphylococcic infection rarely appeared on a death certificate. As indicated before, about one-fourth of all hospitals in this state have acknowledged the occurrence of nosocomial infections. Many of these hospitals are determining the subclinical infection rate and distribution of resistant organisms by culture. Many are establishing the bacteriophage pattern of the resistant organism strain present in the hospital. The typing is done in the bacteriology laboratory of the California State Department of Public Health. Organized research is in progress in eight institutions, in consultation with members of the state and local health departments. All reluctance to discuss staphylococcic infections acquired in a hospital must be overcome before a measure of the extent of infection can be developed. Open discussion is important to education within hospitals. An attempt to develop some reasonable system for reporting or surveillance is under way in California. The California Hospital Association, California Medical Association, California Conference of Local Health Officers, California Association of Bioanalysts, California State Osteopathic Association, California Pharmaceutical Association, Academy of General Practice, Academy of Pediatrics, California Society of Clinical Pathologists, California League for Nursing, California State Nurses' Association, and California State Department of Public Health are being asked to collaborate in studying methods for gathering data. The California Hospital Association and the State Health Department are initiating this program with the support and assistance of these 10 voluntary associations.

The incubation period of intrahospital-acquired staphylococcic infections is an obstacle to obtaining information on morbidity. It is common for newborn infants and mothers to develop their first sign or symptom of infection days or weeks after discharge from the hospital.

Pattern of Staphylococcic Infections.—Pertinent information as to the pattern of staphylococcic infections is available from the observations made in many hospitals: 1. Infection which develops outside and is brought to the hospital for treatment. The Staphylococcus is ordinarily not the hospital or epidemic type. 2. Intrahospital-acquired cross infections. The organism is usually the antimicrobial-resistant hospital strain of staphylococci. Most hospitals share the same epidemic type. 3. Infections which develop after leaving the hospital. The organism is the hospital strain in most instances. 4. Subclinical infections harbored in the nose and throat of hospital personnel and attending staff. Such "carriers" are usually found on services where staphylococcic infections are occurring. By contrast, sometimes none of the nursery personnel carry the epidemic type, while a high proportion of newborn infants may be infected. 5. Contacts, outside the hospital, of discharged patients who have acquired the hospital strain. These occur most frequently in the household. Contact "carriers" may remain subclinically infected for months.

Individual Susceptibility (the Host Factor).—Individual susceptibility or resistance to staphylococcic infection is probably crucial to the problem. Age is the most important single factor. Newborn infants, especially prematures, and the aged are the most susceptible to infections. Adults with debilitating conditions, as found on medical, surgical, and maternity services, lose their usual re-

sistance to the staphylococcus. Normal adults usually possess considerable resistance. However, conditions such as influenza bring the otherwise healthy adult into the susceptibility category of a debilitated or elderly individual. At the present time, the problem of widespread dissemination of antimicrobial-resistant staphylococcic infections due to an epidemic type is the direct concern of anyone planning the study and control of pandemic or epidemic influenza.

Accumulated evidence suggests that infection is perpetuated from patient to patient, however initiated in hospital. It appears to be the susceptible patient—the infant, the elderly, the debilitated—in whom the "hospital strain" becomes implanted, after the patient enters the hospital. The number of hospital personnel "colonized" has been reported to range between 10 and 80%, in different studies.[6b] The length of time in residence in the hospital seems to increase the number of personnel who acquire the infection.

The consensus at present suggests that the newborn nursery is the most important reservoir of the "epidemic type" of staphylococci in a hospital.[8] The strain may become implanted in the nasopharynx of susceptible nursery personnel and subsequently disseminated to personnel in other wards. There are many reasons for believing that staphylococcic infections stem from the nursery. These reasons are implied in the foregoing and described in many papers.[8]

The use of bacteriophage typing of staphylococci, together with the antimicrobial resistance pattern of the strain involved, is helpful to the study of epidemiology within hospitals and essential to such studies after discharge.

Dosage Factor.—The dosage of organisms to which the patient is exposed is doubtless of significance for invasion of staphylococci. The number of organisms in the air of the environment may be second in importance to individual susceptibility. This aspect of environment in hospitals should be possible to control.

Environmental Hygiene

It is established that infections due to the epidemic type of hospital-acquired Staphylococcus pyogenes have been the result of some contact within the hospital. A search for the means by which cross infections are disseminated is necessary. Examples of direct contact between infants are as follows:

1. The ink pad, used in the delivery room to record the footprint of each infant at birth, is used in series. Footprinting is required by law in some states.

2. Penicillin ophthalmic ointment is permitted in most states, in lieu of silver nitrate, for the prophylaxis of ophthalmia neonatorum. The product is used almost universally in hospitals. It is usually packaged in ⅛-oz. tubes, a quantity sufficient for instillation into the eyes of as many as 25 infants in series. Both the ink pad and the ointment have been mentioned as sources of contamination. However, cultures of these items, obtained from hospitals in California where staphylococcic infections were occurring in the nurseries, have failed to reveal the presence of staphylococci.

3. A common comb and common hair brush are used in many hospitals for all infants before visiting hours.

4. A common thermometer is often used for several infants.

5. Sometimes, though an individual thermometer is provided, a common lubricant is used.

6. Crowding in central hospital nurseries is often observed, and is another source of potential exposure. In California the minimum space for nurseries in hospitals established prior to Jan. 1, 1947, is 20 sq. ft. of floor space for each bassinet. Too often this minimum is reduced by the admission of more patients than the hospital quota specifies.

7. The air in a nursery is invariably contaminated with the hospital strain of staphylococci. This has been measured many times. Elsewhere, wherever suppurative wounds occur or other types of serious infections due to staphylococci are present, large numbers of organisms are present in the air.

8. The handling of linen: (*a*) The same cart is often used to transport both clean and dirty linen through devious channels of the hospital corridors, contacting many people as it goes. It is often uncovered. (*b*) A laundry chute is commonly used without the precaution of the double lock to prevent the piston-like action from forcing organisms from dirty linen out into the air of the floor below. In one hospital it was noted that the entry and exit from the linen room were being bypassed, and the linen was being transferred through the windows. When an outside laundry is employed, the exact methods of handling are often not known. The opportunity for contamination would seem great during such transit unless the utmost precautions were taken. (*c*) Autoclaving all linens before they are sent to the laundry from nursery, maternity, and other isolated areas is a desirable precaution. Badly soiled linens should be cleansed in the utility room before autoclaving.

9. The gauze mask: There are potential hazards in incorrect, casual, or prolonged wearing, especially if the wearer places undue confidence in the protection afforded by the mask. The numbers of organisms disseminated are greatly increased by the wearing of masks over prolonged periods. Further, removal of a mask that is wet and growing staphylococci, only to allow it to dangle from the neck and dry before placing over the face again, is obviously improper. This preserves the staphylococci and provides greater dissemination.

10. A common file for cleaning the nails during scrubbing is often used in hospitals. Individual sterile orange sticks should be substituted.

Transfer of Patients from One Service to Another.—The transfer of patients with infections or other diseases from one service to another is common practice in most hospitals. Patients who acquire intrahospital infections should be isolated without transfer. Patients who re-enter a hospital because of a staphylococcic infection acquired there should be returned to the original service. There might be exceptions. Strict isolation technique should be used where suppurative wounds are present. This is standard procedure for postoperative wounds. At least it is possible to "isolate the wound," if not the whole patient. However, as a rule, those who have an infection due to a hospital strain of staphylococci, also have the organism in the nasopharynx, whether recognized or not. The staphylococci are also excreted in large numbers in the stool. Consequently, the potentially dangerous organisms are on the skin. The term "skin dispenser" is descriptive and has been applied to such patients.

In one hospital, patients were being transferred to medical wards for the long-term care of surgical wound infections. This can be an extreme hazard to the chronically ill medical patient.

Recommendations

The recommendations to follow are considered to be basic to good hospital management and to be practical for most hospitals.[10] Principles are stressed. These pertain to all services, including service units. Examples of the measures which seem essential are included as a foundation for the ultimate definitive preventive measures to eradicate intrahospital staphylococcic infections. The principles consist of known methods of isolation and aseptic technique. The foregoing sections are intended to indicate a rationale for these.

Acceptance of personal responsibility for the best possible isolation technique by each member of the hospital staff is fundamental.

Handwashing—Possibly the Most Important Single Control Measure.—The hands should be scrubbed immediately preceding entrance to an isolation unit, and thoroughly washed before any patient care and after care of each patient in the unit. Adequate facilities should be provided in convenient locations to facilitate the "handwashing rule." Foot, knee, or elbow controls for water and a mechanical soap dispenser are recommended.

Soap.—A hexachlorophene cleanser containing the bacterial inhibitor G-11 is suggested.

Gown and Mask Technique.—A gown and mask should be worn by all persons who enter a nursery or other isolated area for short intervals. It is suggested that personnel, whose primary duty is within a nursery or other isolated area, omit the gown and the mask. The gauze mask should be replaced by a clean one after 30 minutes of use.

Washing of Infants.—Bathing infants with a hexachlorophene cleanser, 1 oz., and water to make one quart, has been instituted in several hospitals. The bath is given every other day. Hospitals in California which are known to be using this technique have reported a striking diminution in number of hospital-acquired staphylococcic infections among infants and mothers. A similar trend has been described in other parts of the hospital. A cause and effect relationship is not established, but is suggested. The procedure is rational. Recent experience suggests that a return to bathing of newborn infants, as described, may be helpful in preventing the staphylococcic disease problem and at least should be given a thorough trial.

Handling of Items Inside and After Removal from an Isolated Unit or Area.—The "principles" governing isolation technique are applicable, irrespective of direct contact with patients.

Linen.—Scrupulous attention to eliminate contamination from linens is important. Some of the problems involved have been mentioned.

Bedside Equipment.—Bedside equipment should be thoroughly cleaned daily. All equipment should be issued for the exclusive use of each patient and should be autoclaved before being used by another, except the items which would be destroyed by so doing.

Preparation and Handling of Food.—Special precautions in the handling of food are obviously desirable, particularly the preparation of infants' formulas.

Instruments.—Instruments should not be removed from the isolation units. Careful technique by the attending physicians during all procedures is implicit.

Segregation of Patients on Admission.—The system of separating patients with an infection or suspected infection is an exacting duty of the admitting physician. It has established value. Prevention of intermingling after admission must be strict, if screening is to be effective.

Suspect Nursery.—The use of suspect nurseries has demonstrated the value of early isolation on suspicion. Strict isolation precautions are observed in the suspect nursery, but the central nursery personnel carry on the care of patients there. However, patients should not be transferred back to the central nursery.

Isolation Nursery.—An isolation nursery should be maintained, removed from the area of the main nursery, and have a separate staff.

Rooming-in.—The principle of "rooming-in" is a good one, wherever feasible. There are reports attributing success in terminating outbreaks of staphylococcic infections in some hospitals to the system of rooming-in. In most hospitals newborn

infants are sent to the central nursery for a 24-hour observation period before being placed with their mothers. This gives the ubiquitous Staphylococcus an opportunity for "colonization." The principle of rooming-in does not allow any contact between infants.

Length of Postpartum Residence.—Three days of residence post partum is usual. This is a reasonable time for patients without complications to remain in the hospital. It can be reduced to two days in many instances. Crowding may be diminished in proportion to the length of stay.

Transfer of Patients.—Transfer of infected patients to other services free of staphylococcic infection is theoretically hazardous and to be condemned. There may be very rare exceptions.

Infected Personnel (Carriers).—Some hospital personnel seem to be predisposed to implantation by the epidemic-type staphylococci. The nasopharyngeal "carrier" state is persistent in some individuals. Experience has demonstrated that it is useless, if not harmful, to shift infected personnel from one service to another, especially if the move is to a unit which was free of staphylococcic infection. Experience also has shown that relieving a "carrier" from work entirely is not the answer. When removed from the hospital environment the person may lose the epidemic type of Staphylococcus from the nasopharynx in a time which varies with the host. However, "colonization" will soon take place when contact with the organism is reestablished.

Crowding.—Crowding in nurseries and elsewhere is a common fault in most hospitals. Sometimes it is almost impossible to go between bassinets. Obviously, any crowding of patients at greatest risk is undesirable. Admission of newborn infants to separate units by day of birth may have merit, in that it would separate the "just born" from the "older" infants.

Limitation of Personnel in Nurseries.—The number of individuals who enter any isolation area, especially nurseries, should be the minimum. This is a time-tested precaution and applies to any part of the hospital where there are patients at risk. Such restrictions are effective in proportion to the vigor with which the one in charge enforces the rules.

Visitors.—Each visitor adds to the number of individuals who have contact with the hospital and presumably the dangerous Staphylococcus. Visitors should be limited when infection is present. Not more than two for each patient seems reasonable. Visiting should be limited to the same two individuals to prevent additional contacts. In maternity units, it is suggested that visitors be required to cover their street clothes with a clean gown. Visitors should not approach the patient and infant (if the latter is isolated with the mother) beyond the threshold of the door to a single room, or within 5 ft. of any patient, if more than one is occupying a room. Appropriately placed chairs, readily available gowns, and prominently posted instructions with reasons for the requirements, are helpful. Upon leaving, visitors should remove the covering gown and wash their hands.

Supervision.—Presence of a trained supervisor is vital to accomplishment of most of these recommendations. Experience has shown that extending of nursing responsibilities over several wards or services increases the opportunity for intrahospital transmission of infections. It is undesirable for anyone to cover more than one service. Free substitution of nursing personnel between services, or the system of a "float nurse" or "float supervisor," adds to the number of contacts for both patients and personnel. A method to minimize the number of contacts incident to nursing care can usually be worked out if these factors are considered when making the duty schedule.

Antimicrobial Prophylaxis.—Antimicrobial prophylaxis is not recommended by either local or systemic routes for patients or personnel. Several reports demonstrate the ineffectiveness of administering antibiotics for prophylaxis. Experience has shown that unfavorable effects may result. Therapeutic doses of a drug are occasionally indicated for prevention under unusual circumstances.[11]

Specific Housekeeping Procedures

Public health departments have field representatives who are experienced with equipment, hospital construction, and the facilities necessary for strict isolation technique. Public health nursing consultants can assist in arranging convenient and effective isolation techniques. Certain specific details which are considered important will be noted below. This paper does not propose to describe all elements involved, but to take certain of the more important features for examples.

Central Supply.—A central supply, which is adequately staffed and appropriately located within a hospital, can develop methods which are very helpful in carrying out the principles of environmental hygiene and isolation. This unit can assist all services. Even the smallest hospital can benefit from an effectively functioning central supply, and existing units in hospitals could be expanded to include more of the services necessary for maintaining protection from intrahospital infections.[12]

Cleaning the Environment.—Cleaning the environment means not only the removal of dust and dirt but, in particular, the use of methods to eliminate or reduce the numbers of antimicrobial-resistant staphylococci and other organisms which are constantly present in the air. If efficient, the methods used can reduce the airborne dose of the dangerous organisms to which all hospital patients are exposed. The measures apply to terminal as well as concurrent disinfection.[13]

Sunlight and Ventilation.—An abundance of sunlight and fresh moving air has probably the best sterilizing effect of any method of cleansing the air of hospitals and their physical structures. Sunning and airing of a room and its contents for a period of 24 hours after a patient has been discharged is effective. Articles which cannot be treated in another manner without harming them should be exposed to the sun and air of the outdoors for 24 hours or more.

Ultraviolet Light and Aerosols.—Controlled experiments with ultraviolet light irradiation or with triethylene glycol aerosol have not consistently reduced the number of infections in hospitals. The methods employed have not been successful in preventing airborne infections due to beta-hemolytic streptococci to any extent. The question of the usefulness of these methods in staphylococcic infections remains open. Further evaluation is required.

Vacuum Cleaners.—The use of a vacuum cleaner in hospitals is not recommended. The bag type acts to disseminate the organisms it picks up. The same is true of a water filter type. There are filters of such dimensions which make it possible to remove bacteria from air passing through a vacuum cleaner. However, these must be maintained in perfect operating condition, and a filter so fine would probably not permit efficient cleaning.

Accumulation of Dust and Dirt.—Regular attention to removal of dust and dirt from overhead beams, suspended lights, and other equipment is a feature of good housekeeping. Bacteria-laden dust accumulating on these structures could be a hazard by increasing the number of airborne bacteria, when much of the material falls at once, due to vibration or a similar reason.

Maintenance of Equipment.—Maintenance of equipment by frequent inspection, cleansing, and repair is as important as obtaining the equipment in the first place. This is particularly true of sterilizers and apparatus for proper ventilation.

Germicides.—The ideal all-purpose germicide has yet to be discovered. After study of the compounds available, it is obviously impossible to state categorically which agent is the best for each purpose under all conditions. It is possible to suggest certain products considered the best for most uses, and thereby to help to reduce the number of germicides which are seen in rows of bottles throughout most hospitals.

The phenolic compounds represent effective germicides for many purposes.[13] These are halogenated phenol derivatives such as "O'Syl" which contains o-phenyl phenol. "Amphyl" is a similar halogenated phenol derivative. "Staphene" is a related germicide containing orthophenylphenol, 2-chloro phenylphenol and p-tertiary amyl phenol with soap, organic detergents, and sequestering agents. "San Pheno X" is somewhat similar. These agents have the advantage of a high phenol coefficient of 10 or above for Staph. pyogenes, a residual bacteriostatic effect up to 7 to 14 days, relatively little inactivation by organic matter, low toxicity, and low cost. They have been used as soap for scrubbing, and in the treatment of patients. The principal use is probably by application to all parts of the environment, per se; the walls, floors, beds, bassinets, and as the last rinse after laundering of linens, blankets, and clothing. The reports of bacteriostatic and cleansing effects are dramatic. The frequent and thorough application of the phenolic germicides in proper concentration has accomplished more toward eliminating airborne bacteria from a hospital environment than any other method.[13] The agents can be used for cold sterilization, where essential, and are not damaging to clothing or rubber goods, such as rubber gloves. They are suitable for the kitchen area as well. They should not be used on brass or aluminum. The use of these phenolic germicides, as directed, is recommended.

Hexachlorophene (G-11) and bithional (Actamer) are the two bisphenol compounds employed for their antibacterial properties on skin in soaps and detergents. "Phisohex" and "Septisol" are examples of commercial products. The compounds are highly bacteriostatic and fungistatic, but with lesser bacteriocidal and fungicidal properties. They are only slightly soluble in water, and are somewhat adversely affected by organic material. However, the repeated use of these substances in a liquid soap or detergent preparation accomplishes a marked reduction in skin bacteria by its residual effect. They are recommended for hand scrubs and in-between handwashing. As mentioned, recent experience suggests advantage to their use for bathing infants.

Quaternary ammonium compounds are widely used as germicides in hospitals. The benzalkonium chloride tincture, 1:1,000 (Zephiran), is an excellent germicide and detergent agent when the alcoholic preparation is used. The tincture is often employed as a rinse after thoroughly removing the soapsuds from hands and arms. The quaternary ammonium compounds have the disadvantage of being significantly affected adversely by organic matter, especially blood and serum, as well as soap. The residual effect of these compounds is not comparable to the phenolic germicides, but is definitely a favorable feature for shorter intervals. The use of any rinse between isolated patients, without washing with a bis-phenol soap or detergent, is not recommended. There are too many variables in maintenance of the solution of benzalkonium and in its use by individuals to justify the hand dip. Alcohol has drawbacks of very similar nature.

Education in Hospitals.—A recently published "Guide for the Prevention and Control of Infections in Hospitals" was prepared in collaboration between the staff of the New York State Department of Public Health and a special committee of the American Public Health Association.[10] The publication is highly recommended.

For the training and supervision of hospital personnel, unremitting attention to the following procedures on a continuing basis, by all supervisory staff, including physicians, is considered essential to adequate fulfillment of the recommendations presented here.

Orientation of New Personnel: Orientation is vital for new personnel when entering any hospital, particularly when an infectious disease problem is present. Orientation must be early but the essentials given informally while "in-service."

Continuing In-Service Training Program for Personnel: A continuing program of in-service training is almost essential to effective application of the techniques learned earlier during orientation. This in-service training, to the greatest extent possible, should be carried on in the course of daily work. There is no substitute for precept and supervision.

Standard Nursing Procedures, Each Shift of the Day: Evidence provided by many hospitals indicates that procedures in nursery and maternity units do not remain uniform throughout the day, which often results in extra personnel contact for patients. A serious attempt to standardize the nursing procedures for all shifts is desirable.

The Preeminent Role of the Hospital Physician Staff.—The organized physician staff of hospitals is responsible, with the administrator, for directing the medical technical aspects of patient care. The problem of intrahospital antimicrobial-resistant staphylococcic infections, attended by its community-wide implications, is considered second to none at this time. It is a conviction that progress toward solution of this serious problem is largely dependent upon the vigor with which the medical staff pursue every avenue of approach in the hospital, and as individuals. The leadership and active participation of the practicing physician is essential to the effectiveness of all measures for control. There is justification for intrahospital and perhaps action of a county medical society committee to direct the use of antimicrobial agents, and implement the preventive efforts of the hospital administrator and chiefs of professional services.

While secondary to the practicing physician staff of hospitals, departments of public health can offer important assistance, through consultation, in the effort to control infections due to resistant strains of staphylococci. The variety of technical detail involved can be supplied by departments of public health.

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STAPHYLOCOCCI IN HOSPITAL-ACQUIRED INFECTIONS

TYPES ENCOUNTERED IN THE UNITED STATES

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Hospital-acquired infections due to antibiotic-resistant strains of Staphylococcus aureus present a problem that has become increasingly serious in recent years. It has been demonstrated by numerous investigators that antibiotic-resistant staphylococci have become well established in the hospital community.[1] They are harbored by some of the carriers of staphylococci among the professional personnel (especially members of the medical and nursing staffs); they may colonize some of the patients who, in turn, become nasal carriers; and they sometimes may be found in the physical environment of the ward or nursery, for example in the dust or air, or on bedding or furniture. The established "hospital" strains, subject to ready dissemination within the confines of the institution, thus represent a reservoir which serves as a constant, potential source of cross infection. Bacteriophage typing has shown that in the majority of instances the staphylococci that are responsible for cross infection in any one institution are confined to a relatively limited number of strains. In the event of an extensive outbreak of cross infections, a single strain of a specific phage pattern often is found to predominate or occasionally to be responsible for essentially all cases of infection.

It has been a universal observation that the majority of antibiotic-resistant staphylococci belong either to the broad phage group III [2] or to "type 80/81."

Staphylococci that were specifically susceptible to phage 80 were described in 1955 by Rountree and Freeman,[3] and strains of "type 81" by Bynoe, Elder, and Comtois in 1956.[4] Phages 80 and 81 appear to be closely similar,[4] and for practical purposes strains lysed by either of these phages may be regarded as being identical. In the United States, staphylococci exhibiting the patterns 52/42B/81 or 52/42B/80/81 have been encountered with increasing frequency. Investigations by Blair and Bynoe [5] indicate that the phages 52 and 42B employed for typing in the United States have undergone a slight variation, to the extent that they are capable of lysing strains of "type" 80/81. There appears to be little doubt that cultures which give the patterns 52/42B/81, or 52/42B/80/81, or 80/81 are essentially identical, and they will be referred to here as type "80/81," the designation given to them by the International Typing Reference Center.

From the Laboratory Division, Hospital for Joint Diseases.
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Next in order of frequency of antibiotic-resistant staphylococci are those of group I; resistant strains of groups II and IV, in that order, are considerably less common and account for only a small fraction of the antibiotic-resistant staphylococci that are now being seen.

Types Encountered Before 1954

Published reports of the types of Staph. aureus encountered in U. S. hospitals are at present not numerous, for staphylococcic phage typing has been employed extensively in this country only since about 1953. However, the available information is significant, particularly because it indicates that the strains that have been isolated from hospital-acquired infections and from carriers during the past few years are closely similar to those found in other parts of the world. In reports of the study of over 500 cultures of coagulase-positive Staph. aureus each, Knight and Holzer,[1d] Jackson, Dowling, and Lepper,[6] and Fusillo, Roerig, and Ernst [1e] found that group III strains predominated in the typable cultures isolated in three large general hospitals. The incidence and phage patterns of the cultures are shown in table 1. In frequency of appearance, the group III strains were followed by group I and group II, in that order. Results comparable to these observations were reported in 1953 by Blair and Carr.[2a] It is of interest to note that during approximately the same period a similar distribution of staphylococci among the several phage groups was observed in Canada.

Bynoe, Elder, and Comtois [4] reported that in a hospital in Ottawa between March, 1953, and March, 1954, group III staphylococci predominated (47.1%) in cultures from infected wounds, and in nose and throat cultures of student nurses or of nurses on active ward duty. Type 81 predominated in such conditions as boils, breast abscesses, and carbuncles, being responsible for 50% of the infections. Other types were less common, group I showing an incidence of 2% and group II of 6%.

Some published reports have also described outbreaks of staphylococcic disease in the United States in which Staph. aureus of a specific phage type was regarded as the primary etiological agent. An outbreak of infections in a nursery due to penicillin-resistant Staph. aureus was reported in 1951 by Felsen and his associates [7]; staphylococci isolated from the lesions were phage-typed in the writers' laboratory. It was found that two-thirds of the cultures isolated from lesions were of type

52A. With phages supplied by the writers, Dr. Weil subsequently found that 50% of the nurses who attended the babies harbored the same strain in the nasopharynx or on the skin, and that 63% of cultures of the furnishings in the nursery also yielded staphylococci of type 52A. The fact that this strain was encountered in only 3% of cultures of Staph. aureus recovered from a variety of infections in other parts of the hospital suggested that type 52A was endemic in the nursery. In a series of breast abscesses, Sawyer and Walker [9] found that 66% of their cultures of penicillin-resistant Staph. aureus were of type 52A. The results of both of these studies are closely similar to those reported by Barber in England.[8]

Sherman, Porter, and Eisenberg [10] reported that in a series of 13 breast abscesses due to penicillin-resistant staphylococci in the Philadelphia General Hospital, 9 (69%) were due to staphylococci showing the pattern 52A/79. The four other infections were due to strains of group III, three being closely related and distinctly different from the fourth. An epidemic of staphylococcic infections which occurred among infants and nursing mothers in the University Hospital in Columbus, Ohio, was reported by Shaffer and his associates.[11] All of the 61 cultures of Staph. aureus isolated from neonatal infections and from breast abscesses in nursing mothers were found to give an identical phage pattern, 52/42B/47C/44A. It was found also that an appreciable number of the personnel in the nursery were carriers of the epidemic strain.

The problem of staphylococcic cross infection, which is particularly serious in some hospitals, suggests that it would be advantageous to learn something about the types of Staph. aureus and the distribution of strains that are now being encountered in the United States. With this in view, we sent letters in October, 1957, to 30 laboratories in the United States where a phage typing service had been established, requesting information about the phage types and antibiotic sensitivities of the staphylococci that were encountered during the past year. In eight laboratories insufficient work had been done to supply significant data. Information was obtained from 18 laboratories, representing about 34 hospitals. A number of reports were based upon the study of several hundred cultures each, and some included significant surveys of hospital personnel as well as cultures from lesions. Additional information was derived from the examination of sets of from 6 to well over 100 cultures that had been submitted to this laboratory for typing from about 20 institutions. It is believed that data from a fairly good cross section of the country are provided by the information from these several sources, which represent various geographical areas and which consisted of a number of general hospitals, two Veterans Administration hospitals, and city, state, or federal public health laboratories to which cultures isolated during outbreaks of staphylococcic infection in hospitals had been submitted for phage typing.

From this survey it would seem that the following conclusions are warranted concerning the occurrence of phage types of Staph. aureus in hospitals in the United States at the present time. In the majority of hospitals a relatively limited number of strains, many of them antibiotic-resistant, appear to account for most of the cross infections. Frequently two or three of these strains predominate among the cultures isolated from lesions, that is, they are encountered more often than strains of any other phage pattern; such strains may represent from about 35 to 60% or more of all cultures of coagulase-positive staphylococci that are isolated.

The predominating strains would seem to be responsible for most of the "endemic" infections, which occur more or less constantly but do not ordinarily assume the proportions of an outbreak. Much less frequently, strains of varied types are encountered and no one strain predominates. In the presence of an outbreak of staphylococcic infections, a strain of one phage type usually is found to be responsible for all or nearly all cases that occur within a given period of time. An outbreak may be superimposed upon the usual endemic infections that are due to staphylococci of varied types. Not all of the information that was received in reply to our inquiry was amenable to reproduction in statistical form. However, from these reports some representative data have been selected to illustrate the phage types and antibiotic sensitivity of strains that are currently being encountered (table 2).

TABLE 1.—*Phage Patterns in Group III Encountered in Hospitals Prior to 1954*

Authors	City	Incidence of Group III Strains, %	Phage Patterns
Knight and Holzer[14]	New York	58.5	6/47/VA4; 47; 6/47; 6/VA4; 47/47C/VA4; 7; 47/3C; 42B/47C; 42B/47C/42D/42E*
Jackson, Dowling, and Lepper[6]	Chicago	47.9	7/53; 53; 47/53; 54†
Fusillo, Roerig, and Ernst[15]	Washington	67.9	7; VA4; 47/73/75; 47/53/54/75; 47/53/73; 53‡

* Listed in descending order of frequency.
† The "predominant" patterns.
‡ The "most frequent" patterns.

Staphylococci belonging to the broad phage group III continue to account for an appreciable proportion of "hospital" strains, and to comprise a significant number of the antibiotic-resistant staphylococci. In most hospitals they serve as the constant source of endemic infections, and in some they continue to be responsible for the greater part of the cross infections. In one hospital, for example, staphylococci showing the pattern 53/VA4 were a primary cause of cross infection in the surgical wards, and were harbored in the nose by members of the professional personnel. In two other hospitals, strains of type 7 or 7/77 were responsible for

an outbreak of skin infections in the nursery and were found to be carried by the nurses. In the Hospital for Joint Diseases, where cross infections have been no more than endemic in nature, group III antibiotic-resistant strains have predominated in cultures from staphylococcic lesions for the past several years; a characteristic pattern, 53/77/VA4, has recurred constantly in these cultures.

Present Survey, 1954-1957

A striking feature of the survey is the prevalence of Staph. aureus of type 80/81 as a cause of infection in nearly all parts of the country. It has been variously reported as the "predominant strain" or as being responsible for "practically all" of the hospital-acquired infections in many institutions during the past year or two. Type 80/81 is an important cause of serious outbreaks of staphylococcic disease in the newborn and of breast abscesses in nursing mothers. In some instances the outbreaks have necessitated the closing of a nursery, and in all they have required the energetic application of strict aseptic techniques for their control. While considerable attention has focused upon type 80/81 as an etiological agent in neonatal and related infections, it should be emphasized that it is not the sole cause of these infections and that staphylococci of this type have also been reported to be responsible for furuncles, carbuncles, postoperative infections, pneumonia, and various other conditions. For example, Bynoe, Elder, and Comtois found in Canada that staphylococci of type 81 were responsible for 50% of cases of boils, carbuncles, and abscesses.[4] Rountree and Freeman reported that type 80 was the only etiological agent in staphylococcic pneumonia complicating influenza in Australia; strains of the same type also were incriminated in an outbreak of furunculosis in hospital personnel and caused varied other infections.[5]

Comments in many of the reports received by us, as well as the results of phage typing of cultures submitted to this laboratory, fully confirm the ability of staphylococci of type 80/81 to produce varied clinical forms of staphylococcic disease. While type 80/81 at present is primarily responsible for hospital-acquired infections, the reports indicate that it has been implicated in some primary infections that were acquired outside the hospital and that it may be transferred to family contacts by a patient after discharge from the hospital. As has been pointed out by Ravenholt and LaVeck,[12] staphylococcic disease has now become a community problem in which the hospital plays a significant role.

It would appear that Staph. aureus of phage type 80/81 is highly infective and possessed of more than ordinary virulence. Reference was made by Rountree and Freeman of the unusual clinical severity of furuncles or of infections of minor lacerations, and of the marked persistence of carriage of this type by some individuals. Although most forms of staphylococcic infection have not ordinarily been regarded in the past as occurring in epidemics, in the usual sense of this term, this apparently new strain must be considered as truly an "epidemic" variety, both because of its ease of dissemination and because of its responsibility for the sudden, almost explosive, appearance of infections in an institution. Strains of this type present a challenge and an opportunity to the bacteriologist for fundamental investigation on the nature and mechanisms of pathogenicity of the staphylococci.

The dissemination of type 80/81 in the United States since 1954 appears to have been wide and rapid, for it is now reported, and has been encountered by us in cultures from, essentially all parts of the country. In 1955 an outbreak of breast abscesses in a large general hospital in the east was due predominantly to staphylococci of type 52A/79; in over 100 cultures from patients and personnel submitted to us for typing no strains of type 80/81 were encountered. In the same hospital in 1957, 18.4% of cross infections occurring in the surgical wards were found to be type 80/81. The first strain of type 80/81 from an infection (a soft tissue abscess) in the Hospital for Joint Diseases was isolated by us in late 1955. Subsequently the incidence of this type among coagulase-positive staphylococci

Table 2.—*Representative Phage Patterns and Antibiotic Resistance of Staphylococci Encountered in Hospitals*

Hospital	Phage Patterns	% Resistant to Antibiotics*
1 Predominant	53/VA4	P-80; T-50; S-80; E-37.5; Ch-25
	44A	P-25.5; T-17.8; S-32; E-8.3; Ch-35.7
Less common (in descending order)	7	P-16; T-8.3; S-8.3; E-8.3; Ch-41
	77	P-25; T-50; S-37.5; E-12.5; Ch-12.5
	47/53/54/77/VA4	P-25; S-25
	3C	sensitive
	80/81	P-33; T-66; S-33
2 Predominant	80/81	P-24.6; E-6.9; N-42; "other" - 68
Less common (in descending order)	53/77/VA4; 7; 77; 53; 53/77/VA4	P-10.7; E-12.8; "other" - 42.6
	52/80/44A; 52A; 79; 29/52/80/44A	P-23.7; "other" - 32.6
	3A; 52B	P-3.5; "other" - 10.5
3 Predominant	80/81	"Resistant to penicillin, tetracyclines and streptomycin"
Less common	Group III strains	"Most often associated with resistance"
	Group I strains Group II strains Group IV strains	"Most strains sensitive." When resistance occurred, it tended to be to penicillin
4 Predominant	80/81	P-99; T-98; S-99; E-95; Ca-48
Less common	53/77/VA4	P-65; T-63; S-50 E-23; Ca-54
5 Predominant	80/81	P-96; T-96; S-61; E-3; Ch-3
Less common	47/53/54/77/VA4	P-88; T-88; S-88; E-57; Ch-13
6 (Hospital for Joint Diseases) Predominant	53/77/VA4	P-90; T-80; E-45; Ca-20
Less common	80/81	P-98; T-89; E-44
	47/53/54/75/VA4	P-98; T-82.3; E-24
	52A/79	P-60; T-15

* P-penicillin; T-tetracyclines; S-streptomycin; E-erythromycin; Ca-carbomycin; Ch-chloramphenicol; N-novobiocin.

isolated in the hospital rose in 1956 to 5.3% and in 1957 to 26%. The rapid establishment of type 80/81 as one of the predominant strains in this hospital is the more significant when it is realized that its incidence among the typable strains was 13.7% during the first six months of 1957, and 38.5% during the last half of the year. Since 1955, the incidence of group III strains in this hospital has dropped from 35% to about 26%.

Carriers Among Hospital Personnel

The incidence and types of staphylococci encountered among hospital personnel are of significance in relation to the probable contribution that these individuals may make to the reservoir of hospital strains. In general, carriers of staphylococci among the personnel harbor a greater variety of strains, as shown by the phage patterns, than are found to be responsible for cross infections. This could be expected when one considers all categories of hospital employees as a group, for many of these individuals have little or no contact with the patients in their daily work, and they can be regarded as generally representative of the population at large.

Carriers of the predominating strains, however, are more numerous among the members of the professional personnel whose work requires repeated direct contact with the patients, i. e., the medical and nursing staffs. The majority of the current reports have stated that the strain or strains of staphylococci found to predominate in cross infections were also found to be carried by the professional personnel. The correlation is especially close when applied to persons who work in a department (such as the nursery or in surgery) where an outbreak is actually in progress. Exact figures of the incidence of carriage of an epidemic strain by the professional personnel were usually not given. However, in one hospital 6.7% of the typable strains isolated from carriers among the personnel of all categories were of the same phage type as that which caused the great majority of cross infections.

Sherman, Porter, and Eisenberg [10] reported that 12% of the personnel working in a maternity department where a series of breast abscesses had occurred harbored a strain of Staphylococcus which had been incriminated as a cause of the infections. Shaffer and his associates [11] found that at the time of an epidemic 11 (17.7%) of 62 carriers of coagulase-positive staphylococci in the personnel harbored staphylococci of the same phage pattern as the epidemic strain. Seven of these, or 11.3% of the carriers of staphylococci, also exhibited the typical antibiotic pattern of the epidemic strain; these seven presumably were carriers of the strain responsible for the epidemic. It may be suggested here that the degree of direct contact of the carrier with the patient, and the infectivity of the strain which he harbors is more important than the actual number of individuals who harbor the epidemic strain. Barber and Burston [18] described the onset of severe infections in a nursery a few days after a nurse came on duty who had a boil due to type 52A; prior to her duty, staphylococcic infections had been rare and minor, although 45% of the babies and 26% of the nurses had been shown to harbor a strain of type 52A.

Resistance to Antibiotics

The general relationship between phage grouping and resistance to the antibiotics observed in other parts of the world is confirmed by the reports published in the United States.[14] The broad phage group III comprises the majority of strains, often 80% or more, that are resistant to one or more antibiotics; in descending order of frequency, lesser proportions of resistant strains are found in groups I, II, and IV. The responsibility of resistant staphylococci for serious outbreaks of infection was demonstrated in the reports of Felsen and associates,[7] Sawyer and Walker,[8] Sherman, Porter, and Eisenberg,[10] and Shaffer, Baldwin, Rheins, and Sylvester.[11]

The present survey indicates that the majority of strains that are now encountered in hospital cross infections in the United States usually are resistant to penicillin, streptomycin, and the tetracyclines. The incidence of group III strains resistant to these antibiotics is variously reported as from about 60% to 88%. From about 70% to 98% of type 80/81 strains similarly are resistant to these antibiotics. Occasional strains of group III or of type 80/81 were reported to be resistant to penicillin and streptomycin but sensitive to the tetracyclines or, less frequently, resistant to the tetracyclines and sensitive to penicillin; rare strains exhibiting these antibiotic patterns also have been isolated by us in this hospital. The penicillin-streptomycin-tetracycline-resistant strains sometimes also show resistance to erythromycin; the incidence of erythromycin-resistant strains varies considerably from one institution to another and would appear to be related to the extent to which the antibiotic is used therapeutically. The incidence of strains of all phage groups that are resistant to chloramphenicol usually was reported to be less than 10%, but was as high as 25% in one hospital. Nearly all strains of all groups were reported to be sensitive to bacitracin, carbomycin, neomycin, and novobiocin. When polymyxin B was used for sensitivity tests, all strains tested were resistant to this antibiotic.

The incidence of group I strains resistant to penicillin and the tetracyclines was reported to be from about 16% to 33%; occasional strains were resistant to streptomycin or chloramphenicol, and essentially all were sensitive to the other antibiotics in common use. Less than 10% of group II strains were resistant to penicillin, streptomycin, the tetracy-

clines or chloramphenicol, and were sensitive to other antibiotics. Group IV strains were rare and none was found to be resistant to antibiotics.

Summary

From information supplied by a number of laboratories in the United States, and as a result of phage typing of several hundred cultures submitted to this laboratory, it would appear that at the present time strains of Staphylococcus aureus that the responsible for hospital-acquired infections in this country are predominantly members of the broad phage group III or of type 80/81.

A large proportion of group III strains and nearly all strains of type 80/81 are resistant to penicillin, the tetracyclines, and streptomycin. Resistance to erythromycin may also be encountered, but varies considerably from one institution to another, while resistance to chloramphenicol is reported in most hospitals as generally less than 10%. The majority of strains of the above types have been reported to be sensitive to bacitracin, carbomycin, neomycin, and novobiocin.

Staph. aureus of type 80/81 has become widely disseminated in this country during the past three or four years, and is at present responsible for many serious outbreaks of hospital-acquired infection. While its etiological relation to neonatal infections and breast abscesses has received particular emphasis, this strain also is the cause of a variety of clinical forms of staphylococcic disease, notably furuncles, carbuncles, pneumonia, and infections of surgical wounds.

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HOSPITAL HAZARDS OF STAPHYLOCOCCIC SEPSIS

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The medical profession is dedicated to saving life, which is both dramatic and satisfying. Somehow preventing death is less dramatic and apparently much less rewarding. Nonetheless, the report of Finland and Jones [1] from the Boston City Hospital indicated that many lives may be saved in hospitals by controlling staphylococcic infection. They claim not only that major and minor staphylococcic infections are endemic in large hospitals but also that the Staphylococcus is a leading cause of death. We decided to investigate this problem in our hospital. We asked ourselves whether their "ward-round survey" was reliable and what area of the hospital had the most patients affected by sepsis.

First Clinical Survey

We made a pilot study such as can be done easily in any hospital. During a period of 36 hours we made ward rounds on all the hospital wards. As this was done just before Christmas, 1956, the total number of patients was low (634) due to an annual holiday slump, compared to the normal average (756). The charts on the ward were reviewed with the resident, and the patients were visited with the resident or the nurse. Pus-forming lesions the size of a boil or larger were noted. These lesions were counted as being caused by staphylococci if these organisms had been isolated within the period from 30 days before the survey until 30 days afterward. In addition, lesions were included only if they maintained continuity between the time of culture and the time of the survey.

Results.—Sixty-four patients had staphylococci in their lesions before or after the survey. Six other patients had apparent staphylococcic infection but no culture. They suffered from osteomyelitis (two patients), mastoiditis after previous staphylococcic otitis media, breast abscess, generalized furunculosis, and pustular infantile eczema. This makes a total of 70, or 11.1%, of the 634 patients who had pus-forming staphylococcic infections. The sites of these cultures or lesions are shown in table 1. It may be argued that the vast majority of these lesions might be benign; however three weeks after the survey it was found that 6 of the 64 patients had died. Reference to the autopsy records showed that staphylococci were at least a contributory cause of death in four.

Thirty-four of our 70 acquired their staphylococcic disease after admission, as judged by a careful study of the history of the onset of the infection. As histories were often inadequate regarding this, 34 must be regarded as a minimal estimate.

We believed that steroid therapy might be a precipitating factor in many of these infections, but only 2% of all patients on the first survey were receiving such drugs. None of the patients with staphylococcic infections in this study had had steroids recently. Six patients in the second survey, however, were on steroid therapy and three had staphylococcic infection, one a septicemia.

Although a primary diagnosis of infectious disease had been made by the attending physician in 18% of the patients, a total of 35% of the patients were receiving chemotherapy (sulfonamides, nitrofurantoin [Furadantin], or antibiotics). It appeared that most antibiotics were being used in the hope of buying safety. That this hope was false is suggested since many patients developed staphylococcic infections while taking antibiotics.

TABLE 1.—*Type of Staphylococcic Disease Found in Clinical and Autopsy Surveys**

Site of Culture or Lesion	Survey 1	Survey 2	Autopsy Survey (predominant lesion)
Skin and burns	19	15	...
Wound infection	10	4	...
EENT	12	1	...
Lung	9	3	53
Genitourinary tract	4	...	3
Septicemia	2	1	26
Endocarditis	...	...	2
Bone	9	2	...
Miscellaneous	5	3	5

* 634 patients in 1st clinical survey; 206 in 2nd clinical survey; 534 autopsies in autopsy survey.

Staphylococcic sepsis is not confined to any one area of the hospital, as is shown by the distribution of the infections throughout the services (table 2). Also shown in table 2 are the percentages of the patients receiving chemotherapy on the day of the survey.

We were encouraged by the results of this survey to make a more detailed inquiry to try to extend these findings.

Second Clinical Study with Bacteriological Studies

Methods.—A study was done in June, 1957. The surgical and medical wards (206 patients) were chosen as wards with a high endemic staphylo-

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coccic infection rate on the basis of the first survey. The Psychopathic Hospital (42 patients) and the Hospital School for Severely Handicapped Children (95 patients) were chosen as representative of places likely to have low rates, as infectious cases are excluded. During this study swabs were taken on all wounds and lesions discharging visible pus. Nasal swabs were taken. Certain lesions already cultured that week were also accepted. On this survey 209 members of the staff (physicians, nurses, and attendants) were questioned regarding possible staphylococcic illness, and their noses were cultured. Staphylococci were identified by the appearance and color of the colonies and by coagulase production. Antibiotic sensitivities were done by the disk method.

Results.—Seventeen per cent of staphylococcic infections were found among the patients in the surgical wards and 12% in the medical wards (table 2). However, 7.3% of the medical patients had severe staphylococcic infections in contrast to 2.6% of the surgical patients. The bacteria were obtained from skin lesions (20 cases), the sputum or bronchial washings (4 cases), joint cavities (2 cases), the ear, the gut, the peritoneum at operation, the cerebrospinal fluid, and the blood (1 case each). In patients with staphylococcic infection, 59% were also nasal carriers of coagulase-positive aureus strains at the time of the survey. This history of onset of these infections suggested that a minimum of 38% of them were acquired in hospital. With the exception of the third decade all decades were represented, with most patients being in their sixth decade (table 3). Within a period of three months 10 of the 29 patients died. It is probable that at least three deaths were due to the Staphylococcus.

Various types of antibiotics were in use, but the most frequently used was a proprietary mixture of penicillin and streptomycin. Two per cent of medical patients and 22% of the surgical patients were receiving it.

Only one of the staff stated that he had an active staphylococcic infection. The nasal carrier rates among the staff showed an interesting variation (table 4). The rate was highest in the staff of the General Hospital and lowest in those in the Psychopathic Hospital. That the strains in the nose of the General Hospital staff were probably acquired in the hospital is suggested by the high degree of resistance to the commonly used antibiotics (table 5). It is possible that the staphylococci found in the noses of the psychopathic patients represent the strains found in the general community, but we have not yet had an opportunity to test this hypothesis. Further analysis of these data depend on phage typing, which has not yet been completed.

In the first survey, 5.1% of the 16.5% patients with staphylococcic infection were considered to be seriously ill. In the second survey 4.6% of the 14.7% of the cases were thought to be severe.

TABLE 2.—*Distribution of Staphylococcic Disease and the Use of Chemotherapy on the Different Services of the Hospital*

Service	Patients with Known Staphylococcic Sepsis, %		Patients Receiving Chemotherapy, %		Autopsy Survey		
	Survey 1	Survey 2	Survey 1	Survey 2	No. of Autopsies	No. with Hemolytic Staph. Aureus as Prime Cause of Death	Staph. Aureus as Prime or Secondary Cause of Death, %
Dermatology	13	...	39	...	2	2	100
Gynecology and obstetrics	0*	...	27	...	6	0	17
Medicine	14	12	39	23	157	6	18
Neurology	0*	...	24	...	24	3	21
Ophthalmology	5	...	3	...	None	0	0
Orthopedics	17	...	37	...	14	0	21
Otolaryngology	13*	...	7	...	11	1	18
Pediatrics	15	...	55	...	59	2	14
Poliomyelitis and rehabilitation	15	...	42	...	...†	...	...
Psychiatry	0*	0	0	0	None	0	0
Surgery	17	17	40	43	167	2	16
Urology	4*	...	96	...	28	4	32
Newborn infants	0	...	...	...	19	0	5
Stillbirths and outside autopsies	0	...	...	...	37	...	...

* Cultures taken relatively infrequently on these services.

† Not separately listed in autopsy records.

Pathological Study

The next step obviously was to turn to the autopsy room and see if the Staphylococcus was related to death. To this end the protocols of the 534 autopsies done between Jan. 1, 1956, and Dec. 31, 1956, were examined. Fortunately, it is the custom to culture the heart blood at all autopsies except those in macerated fetuses, stillborn children, and autopsies sent in from elsewhere. When infection is evident at autopsy additional cultures are taken. In those cases where hemolytic Staphylococcus aureus was grown on any culture the anatomic findings were listed and the cause of death was noted in the pathologist's own words. We are biased in regard to staphylococci, and although we were tempted to include more cases as being deaths due to this organism we did not. Other cases where death was designated by the pathologist as being contributed to by staphylococci or not related to this bacterium were separately listed.

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Results.—In the 534 autopsies for 1956, 20 patients were diagnosed by the pathologists as having died from staphylococci disease. In a further 69 cases there had been severe staphylococcic disease, which the pathologists considered had contributed to death. In an additional 70 autopsies staphylococci had been cultured from various areas but, in the pathologists' opinion, they did not appear to be related to death. The sites from which hemolytic Staphylococcus aureus was isolated are shown in table 6. Again the sepsis is spread out among the various services of the hospital (table 2), and is found in the different systems, as shown in table 1.

We believe that this survey and the preceding clinical ones substantiate the findings of Finland and Jones.

TABLE 3.—*Age Grouping of Surveyed Populations from Second Clinical Survey*

Age, Yr.	Patients with Staphylococcic Sepsis	Uninfected Patients, Survey for Nasal Carriers	Autopsy Survey, Staphylococci Considered to Be Primary or Secondary Cause of Death
0- 9	4*	9*	12
10-19	1	8	3
20-29	6	4	2
30-39	2	14	2
40-49	2	21	5
50-59	4	34	17
60-69	11	41	11
70-79	1	33	18
80-89	2	14	17
90-99	2	0	1
Over 100	0	0	1

* Low due to plan of survey.

TABLE 4.—*Carrier Rate of Coagulase-Positive Staphylococci*

	No. Examined		% Nasal Carriers	
Psychopathic Hospital				
Staff	46		33	
Patients	42		36	
Hospital School				
Staff	68		40	
Patients	53		57	
General Hospital				
Staff	95		61	
M.D.'s		38		50
R.N.'s		53		49
P.N.'s & aides		14		86
Patients	206		42	
Total	510			

Report of a Case

The tragedy of hospital-acquired staphylococcic infection is best demonstrated by the following case report.

A 46-year-old female was admitted to the State Tuberculosis Sanatorium in June, 1956. At age 24 she had had an attack of pleurisy, and in March, 1956, a diagnosis of active pulmonary tuberculosis with cavitation and fibrosis of the right lung was made. The sputum was positive for tubercle bacilli on direct smear. Treatment with isoniazid and para-aminosalicylic acid was started in March and streptomycin was added in June. She did well and her sputum converted. Severe bronchiectasis of the right lung and mild bronchiectasis of the left lung were present, however. A right pneumonectomy was recommended and carried out in December, 1956. Postoperatively for four days she was well, then 300 cc. of bloody fluid was aspirated from the right pleural cavity. On the sixth and seventh postoperative days she appeared to be in shock and developed auricular fibrillation. She became apprehensive and dyspneic. Due to respiratory acidosis she was treated in a respirator and a tracheotomy was done. On the 13th postoperative day the anterior portion of the thoracotomy wound broke down. An empyema was drained and the culture of the purulent material grew hemolytic Staphylococcus aureus. She was treated with oxytetracycline (Terramycin), with some benefit. On the 23rd postoperative day she developed cardiac failure. A pericarditis was suspected, but a pericardial tap was negative. The usual treatment for cardiac failure was not effective. She had a fever of 100 to 101 F (37.8 to 38.3 C) and a white blood cell count of 14,700 per cubic millimeter. She died on the 38th postoperative day after a rapidly deteriorating course. At autopsy the cause of death was believed to be severe fibrinopurulent pericarditis and septicemia. A small bronchopleural fistula, pneumothorax and

TABLE 5.—*Percentage Resistance of Isolated Staphylococci to Common Antibiotics*

	No. of People Studied	Antibiotics, % Penicillin	Streptomycin	Tetracycline	Erythromycin	Chloromycetin
Infections						
General Hospital patients	28	61	50	39	25	4
Carriers						
General Hospital patients	54	59	30	31	22	0
General Hospital staff	45	67	31	24	4	7
Hospital School patients	30	33	3	0	0	0
Hospital School staff	27	33	30	4	15	7
Psychopathic Hospital patients	15	13	13	0	0	0
Psychopathic Hospital staff	15	40	7	7	7	0
Total	214					

TABLE 6.—*Sites from Which Hemolytic Staphylococcus Aureus Was Isolated at Autopsy*

	Primary Cause of Death		Contributory Cause of Death		Probably Not Related to Death	
	No.	% of Cases	No.	% of Cases	No.	% of Cases
Cases	20	100	69	100	70	100
Blood	10	50	19	27.5	8	11.4
Lungs	13		38		35	
Bronchi	5	14* 70	12	47* 68.1	11	40* 57.1
Trachea	2		7		4	
Pericardium	2		1		0	
Kidney	4		6		5	
Bladder	0		2			
Other		12* 60		21* 30.4		18* 25.7
Pancreas			1			
Spleen	1				1	
Mouth	1					
Wounds	2				2	
Myocardium	1				1	
Empyema	2		1			
Lymph Node	1				1	
Brain			2		4	
Peritonium			1		3	
Intestine			1		1	
Heart valves			2			
Pericardium			1			
Abscesses			4			
Ureter			1			
Mastoid			1			
Liver					1	

* Excluding duplicates.

collapse of the left lung with secondary severe respiratory acidosis were also contributory causes of death. Hemolytic Staphylococcus aureus was cultured from the pericardium and heart blood at autopsy.

Comment

Here indeed we have an alarming situation. We need to consider our practices and our safeguards to see what we can do. We are not alone in our troubles, as reports have appeared from all over the world documenting situations very similar to this.[3] Staphylococcic problems are present in any hospital where people take the trouble to identify them. What is more they are spread throughout all services in general hospitals. If you admit patients with septic disease you run the risk of having it spread. This problem of cross infection has been well recognized in children's hospitals for many years, but it has not been so well appreciated in our growing geriatric group of patients. Nor is this problem confined directly to staphylococci. If we eradicate them what will follow? Will it be Pseudomonas or drug-resistant coliforms? The rules of prevention have been known for a long time, but they are obviously not being followed.[4]

The answer of the last 10 years has been antibiotics and more antibiotics. Obviously this has not been successful. Add to this the widespread use of steroids, and we are in real difficulty. Highly trained specialists are having problems with antibiotics and steroids.

If you do not admit infected cases you do not have serious trouble, as is shown by our study in the Psychopathic Hospital; so it appears that the isolation of those excreting pus is indicated. This includes obvious sores and carbuncles but also the asthmatic with purulent sputum and postoperative wound infections. Occasionally children with infection of the ear, nose, or throat are mixed with children needing plastic surgery. This illustrates the current false trust put in antibiotics and also problems of hospital planning.

Staphylococci in pus and blood are very persistent, lasting for periods of years outside of the body; therefore the avoidance of contamination of the patient's environment is of prime importance.

Detection.—Our two surveys correspond reasonably well, and therefore we suggest that a "ward-round" survey, which is possible in any type of hospital, is accurate enough for general use. The detection of carriers is difficult and expensive. When they are found we are not certain of their meaning. Are they merely walking air samplers and do they merely indicate contaminated areas, or are they the source of the prevalent infections? Recently it has been demonstrated that an epidemic of staphylococcic infections can be terminated without removal of the carriers.[5] In the presence of a severe outbreak, however, the expensive study with phages is useful.

Although admittedly woefully inadequate, our analysis of carriers suggests that those with the poorest education in hygiene are the most contaminated. It is also possible that these carriers handle more contaminated dressings than do the rest of the personnel.

Antibiotics.—Antibiotics are too valuable to have them wasted by abuse. A potent mixture of penicillin and streptomycin is being used frequently, perhaps even routinely, to avoid infection. It is doubtful if it contributes anything in this field, because of the large number of staphylococcic strains in hospital which are resistant to these drugs. It may be beneficial to discontinue this practice, but to permit the combination to be used in separate injections for those who need it. Antibiotics are not given with skill and forethought, as frequently the diagnosis of the presence of a bacteriological infection is omitted.

The banning of one antibiotic has been suggested. The difficulties of such a system might be overcome by banning a single drug in rotation for six-month intervals, taking precautions to avoid hoarding. It has not yet been proved, however, that such a system is effective.

Local Applications.—Local pus at present brings the reflex administration of antibiotics parenterally. It is possible that chlorine washes or acriflavine or some other antiseptic solution might be a better answer, when there is no generalized body reaction. Well-planned surgery is frequently needed, as in most cases antibiotics will not cure loculated pus.

Prevention.—The rules for avoiding infection have been known since the beginning of the century or even before that. They begin with the first commandment—Asepsis Please! A general breakdown has occurred in our "aseptic conscience," especially by the insidious development of short cuts, halfway measures, and disregarded violations that physicians and nurses alike have accepted today, which they would not have accepted 20 years ago. The problem can be best appreciated by the local notification within the hospital of all staphylococcic disease. Education is necessary, and if started at the top with the physicians it should permeate the whole hospital staff. Ancillary personnel, however, may need special instruction in hygiene as applied to hospital cross infections. Obviously infectious staphylococcic cases need isolation. Perhaps occlusive dressings of wounds, the wearing of masks, and most important of all the washing of hands would be adequate. Hexachlorophene soap should be handy in all nursing areas. In too many instances our hospitals have inadequate plumbing facilities, and the simple routine of hand washing may be very difficult.

Clean wounds are probably best left open and undressed [4] to avoid the dangers of the infected dressing cart. Another approach is to leave the initial dressing in place for up to 10 days. All

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dirty wounds must be dressed from a special cart. Clean dressing rooms should be strictly isolated and used only for their designated purpose. The use of rubber gloves and masks by all personnel handling clean or dirty wounds is recommended.

The method of decontaminating isolation rooms and particularly blankets and other bedding requires more research. The part played by dust in dissemination needs reinvestigation.

The above regimen may be coordinated by an infectious disease committee in each hospital. In some instances, however, an individual such as an infectious disease physician could coordinate these activities more swiftly than a committee.

Summary

The incidence of staphylococcic sepsis in a large general hospital has been assessed by ward round survey, by bacteriological survey, and by an analysis of autopsies. The ward round method was found to give a reliable estimate of the amount of sepsis present. Pus-forming lesions were present in 11.1% of the 634 patients examined, varying in amount from 13 to 17% of the patients on the major services, excepting psychiatry. A second, more detailed survey confirmed these findings and also showed that nasal carriers of coagulase-positive staphylococci were found more frequently among the staff of these services than among the staff in psychiatry. Aides and practical nurses had a high carriage rate. On all the major services of the hospital antibiotics were used in many more patients than those with known infections. Many infections were acquired in hospital, as shown by the circumstances of onset and by the high resistance of these strains to commonly used antibiotics. At autopsy staphylococci were most often cultured from the lungs. The pathologists considered that 4% of autopsied deaths were directly due to Staphylococcus aureus and that a further 14% of deaths were hastened by this organism. Taking into consideration the autopsy rate at our hospital, this means that, in the year 1956, 129 people died primarily or secondarily of staphylococcic infections.

This study was supported by an Iowa Tuberculosis and Health Association grant and by a U. S. Public Health Service grant.

Dr. J. Roger Porter, head of the department of bacteriology, and his staff provided their records and other valuable assistance. Dr. Emory D. Warner, head of the department of pathology, and his staff gave permission to examine their records.

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4. Cross Infection in Hospitals Committee of the Medical Research Council: Control of Cross Infection in Hospitals, Medical Research Council Memorandum No. 11, London, Her Majesty's Stationery Office, June, 1951.

MECKEL'S DIVERTICULUM.—Sixty per cent of the diverticula that have been brought to our attention have given rise to pathologic conditions; of the four clinical manifestations of this pathologic entity, all but the umbilical sinus are potentially lethal. It would seem wise, therefore, to adopt the policy that all Meckel's diverticula should be excised when seen, whether the finding be incidental or due to symptoms. This policy would . . . be varied if the primary reason for exploratory laparotomy was so serious, and the child was in such precarious condition, that further surgery would endanger the child's life. . . . Simple diverticulectomy is done in those cases in which the diverticulum can be taken off without technically compromising the lumen of the bowel. It has been stated by most persons who have had experience in this field that such removal by diverticulectomy is completely effective because the presence of gastric mucosa is limited to the diverticulum itself and one may reasonably expect no ectopic mucosa to be left after a diverticulectomy. . . . Intestinal resection should be reserved for those diverticula in which simple diverticulectomy would compromise the lumen of the bowel and lead to possible secondary intestinal obstruction.—W. B. Kiesewetter, M.D., Meckel's Diverticulum in Children, *A. M. A. Archives of Surgery*, December, 1957.

ECOLOGIC AND EPIDEMIOLOGIC ASPECTS OF STAPHYLOCOCCIC INFECTIONS IN HOSPITALS

SUMMARY

Alexander D. Langmuir, M.D., Atlanta, Ga.

From the broad ecologic point of view, the staphylococci must be classified among the more successful microparasites of man. Over the past century many of man's worst parasites have been routed either by conscious design through intelligent application of preventive measures or by beneficient coincidence of an advancing standard of living, or by both. The staphylococci remain ubiquitous and constitute one of the serious public health problems of today, particularly among hospital populations. Epidemiologic data do not exist that permit a quantitative evaluation of the true extent of this problem, nor is it possible to determine the trends with any accuracy. Only a broad qualitative appraisal can be made.

Clearly, the biological balance between man and the Staphylococcus is vastly more favorable for man today than it was a century or more ago when sepsis, pyemia, and "laudable pus" were universal hazards in hospitals. It is difficult to exaggerate the importance of the discovery of antiseptic and aseptic techniques in surgery and hospital practice, although it would seem that their importance is not always appreciated or respected at the present time.

More recently the introduction of the antimicrobial drugs has further benefited man in his struggle with the Staphylococcus. Many serious staphylococcic infections respond well to treatment with these drugs. Presumably the virtual disappearance of primary hematogenous osteomyelitis of adolescents [1] can be attributed at least in part to the general availability of antibiotics. However, the total impact of antimicrobial drugs on the staphylococcic diseases has been less impressive than their effect on pneumococcic pneumonia, streptococcic sepsis, and gonococcic, meningococcic, and many of the other serious bacterial diseases. A major reason appears to be that many strains of Staphylococcus are resistant to penicillin and other antibiotics.[2] The staphylococcic infections remain a major infectious disease problem in hospital populations.

From the Communicable Disease Center, Public Health Service, U. S. Department of Health, Education, and Welfare.

Read before the Conference on Staphylococcic Infections, sponsored by the American Medical Association, Cleveland, Nov. 14, 1957.

Groups of Staphylococcic Diseases

These staphylococcic diseases may be classified into four broad groups: (1) impetigo and pyoderma of infants; (2) mastitis of postpartum patients; (3) surgical wound infections; and (4) superimposed infections of debilitated patients.

Pyoderma Neonatorum.—Pyoderma neonatorum has long been known, but the extent and seriousness of the problem is often unappreciated. The modern trend of short periods of hospitalization after delivery often masks the existence of the problem until more serious staphylococcic sepsis brings it to attention. Many outbreaks of staphylococcic impetigo, directly traceable to dissemination in a newborn nursery, are accompanied by a significant proportion of serious cases of breast abscess in infants, and even fatal septicemias and staphylococcic pneumonias.[3] The recent recognition of "epidemic" strains of antibiotic-resistant staphylococci in association with these outbreaks deserves special attention.[4]

Mastitis and Breast Abscesses.—Mastitis and breast abscesses in postpartum patients have occurred in serious numbers in association with outbreaks of pyoderma neonatorum.[5] The source of infection in a direct chain from infant to mother has been clearly demonstrated in several outbreaks. The evident hazard is to nursing mothers in contrast to the absence of a problem for mothers of formula-fed infants. This fact is considered by many to be a serious contraindication to breast feeding.

Surgical Wound Infections.—Surgical wound infections like pyoderma neonatorum are sometimes mild, but too often serious. Unless consistently searched for and reported, their frequency and significance may remain unappreciated. Surveys show the seriousness of the problem.[6]

Superimposed Infections of Debilitated Patients.—Chronic illnesses of a wide variety clearly predispose to the occurrence of staphylococcic infections that contribute at least in a minor degree and often to a major degree in the total disability and even as a cause of death. Presumably the general lowering of normal defense mechanisms of the body in these debilitated patients permits the establishment of the Staphylococcus or its invasion of the tissues. Recent surveys reveal the extent and seriousness of this type of staphylococcic infection.[7]

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Comment

The sources of staphylococcic infections are to be found in the hospital environment, both among the patients and among the attendants, including the physicians. Dressings from open infected wounds, purulent discharges, or draining sinuses are notorious sources of large numbers of bacteria.[8] These cause contamination, not only of the hands of the attendants and the instruments used but also of the air and the total environment. More subtle and perhaps equally dangerous is the infected but healthy carrier among the attendants.[6c] These are impossible to identify without highly competent and specialized bacteriological services, and even with these services detailed epidemiologic investigation is often necessary to incriminate a particular carrier as a source.

The mode of spread of these infections in hospitals appears to be manifold and complex. Contact infection clearly explains the breast abscess in the nursing mother from the nursery-infected infant. Generally, in the hospital environment, failure of strict asepsis can lead to a limited number of contact infections of all types, but outbreaks have occurred, continued, and recurred under circumstances where reasonable precautions have been rigidly followed. Airborne infection through contaminated dust is clearly one mode of spread that must be considered. In many situations the mode of spread may remain obscure. More intensive research and new and better tools for epidemiologic investigation of outbreaks are needed.

The control of staphylococcic infections in hospitals may be exceedingly difficult. Obviously the rigid maintenance of aseptic techniques is the starting point. It has often been necessary to close nurseries to stop outbreaks. The practice of "rooming-in" on obstetric services has been advocated as a measure to reduce the problem. Segregation of newborn infants to separately ventilated small rooms within the nursery may reduce the risk of exposure. Search for and removal of a dangerous carrier from the medical, nursing, and attendant staff should be carried out. The use of antibiotic prophylaxis has often been resorted to as a necessary expedient but clearly does not provide a basic solution to finding and eliminating the source of infection or interrupting the existing mode of spread.

No ready solution is apparent to the problems that staphylococcic infections pose to the surgeon, obstetrician, pediatrician, nursing supervisor, hospital administrator, epidemiologist, and health officer. It is clear that much more study and research is needed. The procedure adopted in some institutions of appointing a standing committee of the medical staff to study and report on hospital infections merits careful consideration. Such a committee must receive full support of all groups in the hospital, and must be backed by competent, well-staffed, and well-supported laboratory services. Epidemiologic guidance and consultation are essential to an organized control program. The concerted effort of all members of the medical and health professions will be needed for the eventual solution.

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NEW AND NONOFFICIAL DRUGS

MAKING its appearance for the 32nd year, the 1958 edition of the annual publication of the A. M. A. Council on Drugs is now available from the J. B. Lippincott Company, Philadelphia, under the revised title, New and Nonofficial Drugs (N. N. D.). The first 51 editions (1907 through 1957) of this well-known authoritative source of scientific information on newer drugs were published under the title, New and Nonofficial Remedies (N. N. R.), and under the former name of the Council, the Council on Pharmacy and Chemistry. The changes in the title and in the name of the Council have been subsequently instituted and editorialized in THE JOURNAL.[1] It therefore seems appropriate to call to the attention of physicians the availability of the 1958 edition of the Council's publication.

Like its predecessors, New and Nonofficial Drugs includes cumulatively in bound, classified, and indexed form all Council monographs and supplemental statements on commercially available drugs which have appeared in THE JOURNAL and which have not been included in the book or in official publications for more than 20 years. Accordingly, no physician who wishes to have accessible for convenient reference all current statements on individually available drugs as evaluated by the Council should be without a copy of this handy source of information. The 1958 edition contains 48 new monographs on drugs and, altogether, monographs for more than 600 individual therapeutic, prophylactic, and diagnostic agents. Chapter and section statements concerning various pharmacological and clinical classes of drugs are also included. In addition to the alphabetic listing of commercial (trade) names with each monograph and in the index, the 1958 edition incorporates, as a further aid to prescribing, a generic listing of available preparations and their sizes or strengths.

Since 1955 the scope of the Council's annual publication has been expanded to include descriptions of unestablished as well as established drugs. This enables the Council to present its views, both favorable and unfavorable, respecting all commercially available individual preparations. Thus, the Council's publication has become a general source of clinical information on newer drugs and no longer is restricted to the description of selected remedies. The revised title of the book serves to reflect more accurately its content of both unestablished and established drugs, including those used for prevention and diagnosis, as well as therapy of disease.

Physicians should take particular cognizance of the scientific procedure by which the Council's annual publication is compiled under its program for evaluation of drugs. When a new drug is placed on the market, the Council A. M. A. Headquarters Staff obtains all available pertinent reports of laboratory and clinical investigations, usually through the cooperation of one or more manufacturers. These data are circulated for review by several consultants selected for their competence in the field of therapy involved. Their opinions are transmitted with the data and a drafted statement of actions, uses, and dosage to a

1. Name of Council and Title of Its Annual Publication Changed, statement of the Council on Drugs, J. A. M. A. **163**: 645 (Feb. 25) 1957. A. M. A. Council and Publication Renamed, editorial, ibid. **163**: 649-650 (Feb. 23) 1957.

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member of the Council, who serves as a referee. The referee, in turn, forwards his comments with a recommendation concerning the statement for publication, for consideration by the Council as a whole. All members acting together are then given an opportunity to review the data and the comments of consultants and the referee, to offer suggestions, and finally to vote on the proposed statement for publication before it is submitted to the Editor of THE JOURNAL. Manufacturers which have furnished data to aid in the evaluation of new drugs are given the opportunity to comment on statements prior to release of the monograph for publication; valid suggestions for modification receive consideration prior to publication. The same procedure is followed in evaluating and publishing statements on additional new uses and routes for administering previously evaluated drugs. The Council's method of operation emphasizes the large amount of work performed by its members and its consultants in providing the information that is included in its column of THE JOURNAL and in New and Nonofficial Drugs. Indeed, the work of the Council insures a thorough, critical appraisal of drugs such as the individual physician could not find time to do for himself.

A further important fact concerning New and Nonofficial Drugs is its annual over-all revision. As new experience and information become available, monographs describing previously evaluated drugs are revised in the light of changing knowledge. Thus, the latest edition is not just the latest style—it is the latest critical information that can be provided by the Council, and it is offered as an A. M. A. service to the medical profession.

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MEDICAL EDUCATION
WEEK .... April 20-26

STAPHYLOCOCCIC INFECTIONS

Staphylococcic infections constitute a world-wide health problem. The long-awaited emergence of antibiotic-resistant strains is providing a serious problem in many hospitals, especially in the nurseries. Elsewhere in this issue a series of seven articles deals with various aspects of the situation. Different factors combined to make this development almost inevitable. For many years physicians had been combating staphylococcic infections with germicidal preparations. Although from the time antibiotics first became available there have been warnings that they were bacteriostatic rather than bacteriocidal, the therapeutic importance of this fact was not always appreciated. Another factor is related to the "bird-in-hand" philosophy. It is only human nature for patients to demand all that is available at that moment. At times such insistence is overwhelming to even the most reluctant prescriber. The attitude expressed in the phrase "after us the deluge" is short-sighted, but many persons find it hard to worry about a future they may not live to see. In the case of the antibiotic-resistant staphylococci, the development came faster than was expected. The fact that antibiotics were given to many patients who had no proved infection undoubtedly did much to hasten the appearance of the resistant strains.

Now that the resistant strains are here, it is important to learn as much about them as is possible. That an impressive start has been made can be seen in the article by Mudd (page 1177). The need for continuing research on this problem is stressed by Langmuir (page 1202). One thing that emerges from this symposium is the fact that aseptic techniques should never be relaxed for a moment in spite of the convenient availability of antibiotics. The modes of transmission of staphylococci are varied and complex, and the organisms are practically ubiquitous. One of the chief sources of danger is the healthy carrier. In addition to asepsis in the operating room and nursery, many housekeeping details in hospital management must be considered. These are aptly presented by Brown (page 1185). Fortunately, a few antibiotics are still effective against staphylococci. How long they will remain so will depend on the wisdom and restraint with which they are used.

ORGANIZATION SECTION

IT TAKES TWO . . .

Gunnar Gundersen, M.D.

It takes two for a good many things in our world today. For example, two heads are better than one; there are two sides to every question; there are two eternities—past and future; it takes two to converse; it takes two to play tennis; two to dance. In American communities it takes two kinds of physicians to promote and pursue the goal of the best possible health for all. It takes one who treats the individual in the community; another who treats the community as an individual.

Neither can ignore his responsibilities to the community and the individual. The private practitioner has responsibilities in prevention, and consequently with mass disease and public health. The public health physician has a long line of responsibilities in epidemiology and health education. He therefore wisely stays out of the field of individual treatment. Like his colleague in private practice, the public health physician knows treatment can be rendered best only in a relationship between doctor and patient which is personal and confidential.

Leadership—the Role of All Physicians

Each physician in public health and in private practice must assume his individual and collective role in community health. That role in one word is leadership. You are qualified to be public health leaders, because you have been trained as physicians. Besides this basic medical education, you have been trained in group leadership, in administration, in handling of budgets, and in the application of educational measures to the persuasion of the public toward actions beneficial to individual health and to the public health. Second, your official position requires you to be a leader. Your responsibilities are defined by law. You take an oath to enforce the law and to do those things which are necessary for the protection and promotion of the public health.

You cannot escape from your role of leadership. To aid you in your work, the law appropriately gives you certain powers. Indeed, you easily could be the most authoritarian official in the entire governmental organization of the United States. Only you can impose a quarantine which restricts the comings and goings of people who have committed no offense. Only you can issue orders under a broad legislative delegation of powers which may seriously curtail the ordinary rights of the individual. In fact, the courts have held that as long as you are fair and reasonable, there is very little limit to your authority exercised for the protection of the public health.

But the wise public health physician knows he must lay aside the cloak of authority if he wants to lead. Instead of issuing orders under the law, he endeavors to persuade in order to be an accepted, not an authoritarian, leader. Where formerly he developed programs and tried to sell them to the community, he now calls community leaders to him and together they plan projects, blending their ideas and judgment, and finally evolving a plan which is an amalgamation of their best ideas. This modern concept of public health is a far cry from the old idea of the health official sitting in his sanctum and deciding under the law what people ought to do and then proceeding to make them do it if he could.

So today the health officer deserves the support of all good citizens and especially of his colleagues in the medical profession. No one can understand so well as the doctor the requirements and the necessities of public health programs. No one can so effectively support a sound public health program as can the medical profession in the community. No one can, by the same token, oppose so effectively ill-considered schemes.

Physicians' Awareness of Responsibilities

Although physicians and medical societies have been criticized for their apparent disinterest in public health, I believe that more and more of them are showing real concern for the well-being and betterment of their home towns.

Certainly the success of public health programs depends, to a large degree, upon the practicing physicians and other medical personnel and medical facilities in the community. A health department unsupported by the medical profession, divorced from the community's hospitals, and alienated from others in the community working toward similar goals is a sorry thing indeed. I believe that any professional group—doctors, lawyers, teachers, engineers, or businessmen—which has failed to recognize its interrelationships with other professional groups is missing a large proportion of its opportunities and falling far short of its obligations.

President-Elect, American Medical Association.

Read before the American Association of Public Health Physicians, Nov. 14, 1957, Hotel Statler, Cleveland.

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The only solution for constructive progress in public health lies in the cordial cooperation of all groups concerned with mutual respect for each other's principles and opinions. Personally, I am proud of the recent work of many medical societies in the field of community and public health service. For example, in Decatur, Ill., a city of 75,000, the physicians of the Macon County Medical Society rallied public support for a sewer bond issue and for a dam to raise the level of Lake Decatur. The measures won by wide vote margins. Some of the plaudits from the citizens were: "If the medical society recommends it, the bond issue must be essential to the welfare of the city." "One of the best things that has happened to this community is the revival of the medical society's interest in public affairs."

In Bronx, N. Y., several years ago the Bronx County Medical Society members waged an on-the-scene battle against Pugsley Creek. They surveyed the foul-smelling, rat-infested, garbage-laden, insect-breeding creek to help persuade city officials that it should be filled in as a serious health hazard. They succeeded. This was not the medical society's only city project. They took up such problems as smoke abatement, safety programs, emergency ambulance service, and others.

In Ohio, the Columbus Academy of Medicine is an excellent example of a group of physicians working actively to solve health problems. Among the academy's achievements have been the setting up of a countywide tuberculosis control program, the reorganization and planning of a child mental health clinic, and the creation of a city health department.

Scores of other examples could be cited. State and county medical societies have interested themselves in accidental poisoning, home safety, retirement homes for the aged, improved refuse control, milk inspection, poliomyelitis vaccinations, Asian influenza, foods and drugs, medical quackery, blood banks, alcoholism, traffic accidents, and many others.

These are a few of the problems for which the physician must feel a responsibility, along with the public health officer and the private citizen. These are the problems that must be attacked in unison, in cooperation, and with a mutual understanding. These are civic obligations. They must be met by all citizens, and especially physicians who are doctors of medicine dedicated to rendering service to humanity.

A. M. A.'s Interest in Public Health

I am proud to say that the American Medical Association in its 110-year history has been deeply concerned with matters pertaining to public health. Without trying to present any long history lesson, let me quickly point out some of the A. M. A.'s work in public health.

The Committee on Public Hygiene was one of the A. M. A.'s first committees to be appointed, and its 1849 report urged an extensive study of the health problems of that era. By 1872 public health had advanced sufficiently to form a Section on State Medicine in the A. M. A.'s Scientific Assembly. State medicine then was defined as "the application of medical knowledge and skill to the benefit of communities." Nevertheless, the name was largely misunderstood by the profession and eventually was replaced by more modern terminology. The Section had various names from 1872 until 1900, when it was changed to the Section on Hygiene and Sanitary Science. Several years later it became the Section on Preventive Medicine and Public Health, and then in 1922 the Section on Preventive and Industrial Medicine and Public Health. Recognizing that the specialty of preventive medicine includes both industrial medicine and public health, the title was changed to the Section on Preventive Medicine in 1955.

Many of the great names in public health also have served the American Medical Association as president over the years. You will recognize such men as Henry I. Bowditch, founder and first secretary of the Massachusetts Board of Health; Thomas M. Logan, founder and first secretary of the California State Board of Health; Joseph D. Bryant, health commissioner of New York; Rupert Blue, surgeon general of the U. S. Public Health Service; and Walter L. Bierring, state health officer of Iowa. These are just a few in the long list of those in the public health field who have served organized medicine so well.

"All Against Evil Only"

These men of public health stayed close to their medical colleagues, and private practitioners in turn stayed close to the public health physicians. Today the A. M. A. seeks that same kind of cooperation. It desires to understand, not just tolerate, public health and public health physicians. That is why the A. M. A. Board of Trustees supported in principle the proposal to form the association of public health physicians and why the A. M. A. gave this group its hearty endorsement.

In the past year the A. M. A. has had two particular occasions to work closely with public health physicians in the nation. These involved the poliomyelitis inoculation campaign and the Asian influenza education program. While I must admit that there were strained relations at times in some areas, the over-all picture of cooperation by private practitioners and public health physicians has been gratifying. Certainly these two programs indicate that outstanding work in behalf of better health for all Americans can be done by men of good will.

I certainly hope that there are no more of my colleagues who look upon the health department as a bumbling, bureaucratic agency interfering in

the medical field. Likewise, I hope that public health physicians do not look upon private medical practitioners as physicians to ignore, circumvent, or hold in contempt. We in the private practice of medicine are not out to take from the community; we are interested in putting back more than our share into the community. We are determined to make our communities better places to live. We are dedicated to the betterment of the health of the community and the people in it.

I would be less than frank if I did not admit there have been times when the medical profession has been heard only when it criticized or opposed certain public health programs. But perhaps the blame is not all on one side. It may be that the health officers have gone ahead on their own without consultation; it may be that the medical profession has not kept in touch with the progress of public health work. Regardless of who has been to blame, the situation has been deplorable in that most differences have been so unnecessary.

In those areas where public health officials and private practitioners have cooperated, the results have been wonderful. Certainly, the benefits of further cooperation are unlimited. To bring about more of this kind of accomplishment, we must eliminate unproductive rivalries and interminable wrangling which do immeasurable harm to our cause and bring public discredit upon both of us. It takes two to feud; two to quarrel. But these same two can unite their efforts; they can pull together; they can work wonders for the people they serve. As Thomas Carlyle wrote: "Men's hearts ought not to be set against one another, but set with one another, and all against evil only."

The following papers were among those presented at the County Medical Societies Civil Defense Conference in Chicago, Nov. 9-10, 1957. This is a yearly conference sponsored by the Council on National Defense of the American Medical Association. Other papers were published in the Feb. 15 and 22 issues of THE JOURNAL.—ED.

CIVIL DEFENSE MOTIVATION

Cortez F. Enloe Jr., M.D., New York

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Why do people yawn whenever civil defense is mentioned? Why don't they think about protecting their own country, themselves, and their own communities? These things they can do something about, instead of worrying about what happened to Zhukov or what Khrushchev said at the last Turkish Embassy cocktail party. Why is all their attention focused on Sputnik, and now Muttnik, and perhaps next week when they put an ape in it, Apenik—things they certainly can't do anything about? And yet this dire and pressing problem of civil defense has such a high boredom rating. Maybe if we try to find the answers to these questions we can get some idea of the problem we face in medical planning for civil defense, and perhaps the very questions will themselves suggest their own answers. Let us see if we can figure out why this is so. Perhaps we are like the internist who said that he had the diagnosis down pat, but did not have the vaguest idea of what to do about the treatment. As physicians, we all know that before any problem can be solved we have to define the problem. So before I attempt to suggest to you how you can arouse people's interest in civil defense, let us see why they are not interested.

First, the people in the United States, by and large, feel pretty hopeless about their ability to provide any kind of protection against atomic bombs and guided missiles. We all know that if you give people every harrowing detail, they become hysterical, cynical, indifferent, or even antagonistic. Perhaps this explains the hand-wringing of the Association of the Atomic Scientists and the attitude of the irresponsible social do-gooders who want to call a halt to everything in atomic energy and whose motto is "Don't worry, nothing is going to turn out all right." Add to this the security of the government, much of it necessary, and it is easy to understand why the public thinks a good deal of the civil defense program is a waste of time. Now add to this the undulating policy of federal agencies that cannot make up their minds about what kind of defense is best. At one time they say that evacuation is the only answer, and then the pendulum swings in the opposite direction to the efficacy of shelters, pausing, as do all pendulums, at dead center, at no program at all. Is it then no wonder that people feel that civil defense is much ado about nothing?

The second reason why it is difficult to interest people in civil defense is that there has been little or no consistency of leadership provided by their governmental agencies. The Defense Department, where, in my opinion, the whole business belongs, acts as if civil defense did not exist. The Federal Civil Defense Administration (FCDA) has not done much to arouse people's interest in the whole prob-

Member of the Committee on Civil Defense of the American Medical Association.

lem although it has had highly competent medical officers assigned to it and a medical advisory committee to the administrator.

Third, if the people knew how protection could be afforded them by a sound civil defense organization—and even if the government provided the leadership and people were given hope that there is, indeed, some place to hide—a large segment of our population would lack interest in civil defense simply because the danger is not imminent. Let us face it: most people do not think about owning a fire extinguisher until the flames are coming out of the attic, but fortunately for us this is a little less true for doctors than for people as a whole. So there you have the three reasons why it is difficult to interest people in civil defense: (1) hopelessness before the weapons, (2) insufficient government leadership, and (3) lack of understanding of the need. These three lacks can give us some valuable clues as to what we can do to arouse the interest that is necessary if we are going to have a working plan for medical civil defense.

Civil Defense as a Medical Problem

It is the third facet of this problem that offers us a clue. I think there is very little that we in the medical profession can do to change the government's attitude, and I do not want to attempt to remove the psychological block that people have about the atomic bomb, but I do think that by one method, somewhat devious to be sure, we can make great forward strides in organizing a medical care program for civil defense. For one thing, we should play down the fact that we are talking about civil defense and talk more about community medical emergencies. I believe the only thing that has saved even the existence of the FCDA has been the work it has done in natural disasters, and I commend the study of its experiences to everyone. The more that we look at the civil defense problem as a problem of medical emergency in a community, the more we are going to be able to interest people in doing the very things that will be called civil defense if there is a foreign attack, and will be called a natural disaster if there is a hurricane. The activities are very similar, so let us train for one, keeping in mind that we are training for the other.

The first thing to be done in any community is to have a civil defense plan, but this plan is no good if it only exists on paper, and if participation of the local government departments is on a voluntary basis. The plan must have teeth in it, and the activities of each department in the local government should be a matter of law. They have done this in San Francisco with splendid results. Secondly, as physicians, we should build our disaster plans around our hospital staffs. The American Hospital Association has given impetus to this by making the existence of a local disaster plan a requirement for accreditation. This is a remarkable and encouraging starting point. If each hospital, from the smallest to the largest, has a working plan for the care of mass casualties, we will have taken a giant step forward in arousing people's interest in civil defense.

Mind you, I said "working plan." By that I mean a plan that has been shown to be functional and good. The only way you can show it as functional and good is by having, at regular intervals, exercises in which the entire hospital staff and the local ancillary services, such as the Red Cross and the Gray Ladies, participate. Participation by the hospital staff must be made mandatory. Decision to participate in the exercises if they feel like it cannot be left up to physicians. They should participate as a requirement for maintaining their staff positions. More community interest will be taken in this program if the hospital board members also have a job to do in the hospital mass casualty program. And think what you can do if you give the wife of each staff member of the hospital an obligation to fulfill in connection with the exercises at the hospital. There are very few doctors who are going to fail to attend a vigorous exercise in the care and handling of the hospital when their wives are down there working all day.

Certainly, the county medical society should have its committee on disaster planning, but this is not a job for the county medical society. The interests are too varied in each of these groups. The hospital is a functioning unit and the chain of command already exists. Furthermore, in the hospital, it is easy to break down any problem into its small parts, so that a large number of people have something to do.

If you would like an example of the method I am suggesting of arousing interest among the people associated with the medical profession in civil defense, read "Exercise 'Operation Rebound'" in the Feb. 15 issue of THE JOURNAL (page 785), a program which was conducted in Houston, Texas, and reflect that from the first 85% of all the people, doctors included, even remotely associated with that hospital were enthusiastically participating in a long and arduous program. As I say, we have a responsibility toward providing emergency medical care; every doctor knows that. So if you want to arouse interest, emphasize the necessity for gaining proficiency in collective medical care in emergency measures and do not become involved in the useless controversy of evacuation versus shelters. Others are working on that problem. Just a month ago the President appointed a group, made up of several very famous men who have been working in great

secrecy on all of the civil defense problems, to handle this as one of its problems. So let us leave that to them.

The more successful you are in developing a hospital emergency plan, the more exercises you can have, the more attention you will draw to this problem in your community, and the more attention you draw to it, the more it is going to occur to people to think about home care. But as doctors, and as men in organized medicine, we must see that to succeed in discharging this responsibility we must stay on the medical mission. We must be organized, so that we will not encounter the situations of confusion which seem so typical of situations in the recent past. For example, in the recent disaster in Kansas City, trucks, station wagons, and private automobiles carried the walking wounded and what should have been litter cases and the dead to the hospitals, and, with but one exception, not a single ambulance was able to get within five miles of the disaster area. Of what use is medical care in such circumstances?

You may encounter this in the natural disaster program of any community at any moment. If we do develop a good medical program for meeting natural disaster, and cooperate with other community services and the local government—a matter in which I am sure you can arouse interest—we will succeed in providing emergency medical care that is useful in peacetime and of absolute necessity in wartime. There is an immense amount of generous, patriotic, and potentially competent volunteer effort that can be recruited for a program under experienced professional direction which has won respect. To recruit it, we have to show that we can carry out our medical mission, and we can only do that through using suitable methods.

COUNTY MEDICAL SOCIETY ORGANIZATION AND ACTION FOR DISASTER PLANNING

Leonard K. Knapp, M.D., Lake Charles, La.

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We experienced a tragic local disaster on June 27, 1957, when hurricane Audrey struck the southwest Louisiana coast. In this disaster there were 534 persons missing and killed; of these 23% were under 5 years of age, and 43% were 17 years old or younger. Of the 337 bodies found, 114 were unidentified. To fully understand how this disaster occurred, one must know something of the geography of the region involved. The disaster took place in the coastal parish (county) of Cameron, La. This is primarily a parish of marsh land, the highest point being 10 ft. above sea level and most being only 0 to 5 ft. Across this parish run two or three ridges which the residents consider "high ground." On these ridges are three towns, Creole, Cameron, and Grand Chenier. Cameron is the county seat. Each of these towns is 5 ft. above sea level.

Certainly part of the blame for the high casualty toll must be placed on inadequate warning. I make no attempt to determine how warnings should be worded or be relayed to the people, but most of the people in Cameron Parish went to sleep on June 26 thinking the storm would arrive in the late afternoon on June 27, and there would be plenty of time to get to "high ground" in the morning. The electricity failed in Cameron about 9 to 10 p. m. on June 26. It was 1 a. m. on June 27 before the forecast predicted the storm would reach the coast before noon. At approximately 3 a. m., 12 hours ahead of schedule, this storm hit, with tides putting the entire parish under water. The high outer ridge, 5 ft. high, trapped the water back inland in the parish, and the winds and water wrecked homes. The water drained away from the coast when the wind and tide subsided, but the inland part of the parish remained inundated for many days. The tide reached 10.5 ft. above mean Gulf level. In addition to this, the waves were estimated by conservative men at 10-ft. height. You can imagine what this, coupled with 110-mph winds, would do to a town 5 ft. above sea level.

The Calcasieu Parish Medical Society (this includes the three physicians practicing in Cameron where there is no local society) has been organizing under civil defense since 1952. I happen to be chairman of the civil defense committee of the parish society and director of the health services for Calcasieu Parish Civil Defense. We have organized along two lines. One for atomic disaster, in which we plan to evacuate the entire target area and utilize schools and hospitals in surrounding areas. This has not yet been put into action.

Our second plan, to be put into use in all natural disasters, explosions, and train accidents, is based on the premise that our local hospitals will be standing, usable, and able to take care of all foreseeable casualty loads. It is the purpose of the health and medical services of civil defense to organize with the aid and assistance of the local hospitals, physicians, nurses, technicians, practical nurses, and other allied personnel in order to better care for the sick and injured and insure the general public health in time of a local emergency. It is as-

Director, Health Services, Calcasieu Parish Civil Defense.

sumed that this plan is a more or less fluid one, adaptable to any of the various anticipated local emergencies, either natural or man-made, but excluding war or atomic attack, in which case the evacuation plan would be put into effect.

Administrative Personnel

The health services are under the direction of a director, who is assisted by a deputy director, and a coordinator. In the absence of the director, the deputy director is in charge. It is the duty of the director to organize all of the various medical personnel and facilities to best care for emergency situations as they may be foreseen. It is the duty of the coordinator to assist and advise the director on civil defense matters, to aid in maintaining liaison among all neighboring hospitals and their administrators, to aid in training personnel in civil defense practices, and to act as a public relations officer.

All physicians in the parish will be assigned to specific hospitals or to aid stations or triage teams. Each hospital has assigned a director and an alternate. The chief of the nursing services personnel is responsible for enlisting the professional nurses, the practical nurses, aides, and all technicians in the program. After enlisting, each of these individuals will be assigned to specific duties. Insofar as possible, these personnel will report to their usual place of duty in the hospitals, and the remaining personnel, who are not ordinarily working in hospitals, will form a pool for assignment to aid stations, triage teams, and for relief or supplement of hospital personnel.

The public health officer and his staff are responsible for maintaining public health standards during any emergency. The health services supply officer is in charge of obtaining all necessary supplies during any emergency. He will work with local drug houses, hospitals, and clinics, and with the civil defense supply service and welfare service in obtaining these. The health services communications officer acts as a liaison officer with civil defense communications service and with local amateur radio operators to supply communications to each local hospital, to the health services headquarters, and to each aid station or triage team.

Our operations during the emergency phase of this disaster may be briefly recounted. We made mistakes, as will be seen later. Yet, we did act in an organized manner. The members of the medical society and nurses and all allied personnel responded wonderfully. Everyone worked to the utmost of his or her ability. Mr. Hinsley has outlined our operations in Lake Charles on the day of the hurricane (see page 1213). He did a fine job in having his hospital prepared for an emergency. For the most part, the doctors were on a standby basis that day, taking care of a few casualties and making a few calls at refugee centers.

Activities in Aiding Devastated Area

At approximately 2400 hours on June 27, 1957, I was notified by the civil defense office that although no direct communications had been established with Cameron, it was felt that the damage there might be considerable, and we were requested to send doctors, nurses, and medical supplies into the area. The civil defense would furnish us transportation at 0400 hours on June 28. Could we get them ready? Yes, I told them we would.

I knew that we would have no trouble recruiting the doctors and nurses, but knowing just what supplies to take without knowing anything about the type of situation we were getting into was a problem. My first thought was to get supplies from the local federal civil defense warehouse, but I was immediately told that these were not available to us. I called Mr. Hinsley and we decided to use some of the supplies in his custody as part of the 200-bed mobile hospital. These were delivered quickly in a large van truck purchased by the Louisiana State Department of Hospitals to move this hospital, and solved our supply problem except for narcotics and some dressings that we rounded together from local doctors' offices and drug stores. We took all the equipment except the major operating room supplies for the 200-bed hospital. These included all first-aid supplies, cots, blankets, small sterilizers, dressings, syringes, and one large generator.

We congregated at 0300 hours and decided to send part of the doctors and nurses by boat and part in the army ducks provided for transportation. At 0400 hours our party was off. I am sure that I speak for the entire staff when I say that we were shocked when we reached Cameron Parish. There was nothing but water and total destruction. Barely a building was left standing in the entire parish. People were still on roof tops, floating on debris, in trees, or swimming, and everywhere were dead cattle and dead people. We had planned to go to Cameron, render some first aid, and then send the people home. It became immediately apparent that the entire parish would have to be evacuated. With this in mind, we decided to set up two aid stations to treat and sort casualties for evacuation, one at Creole and one at the town of Cameron. The party was then divided into two parts.

When our party reached Cameron we found people concentrated in the court house, which was still standing. Dr. Clark had done a remarkable job in rendering aid and comfort to his people. He had been on the job for some 24 hours when our first-aid station was set up. We found Drs. Carter and Dix in Creole continuing to work with everything they had. We set up those two aid stations, in Cameron and Creole, and manned them with shifts of doctors and nurses for the next three days. After

the first day, these were eight-hour shifts, the personnel being relayed by helicopter. These are wonderful machines in disasters of this nature.

In each aid station we tried to organize so that each casualty was examined and given first aid: dressings to injuries, penicillin, and narcotics as indicated. During our first three or four hours' operation we had no food or water to offer them, but this soon arrived. The injured were then evacuated by either boat or helicopter, depending on the merits of the individual cases. Each casualty was tagged.

In Lake Charles, where I had left operations in the hands of my deputy director, Dr. Edmond C. Campbell, things were progressing in a somewhat hectic but not chaotic manner, and by the time I arrived in Lake Charles that first night, things were under control. Refugees arrived by three means: boat, truck, and helicopter. A large reception center was set up at McNeese State College gymnasium, and doctors and nurses were on duty there. The refugees were examined by doctors and nurses, given food and clothing, and their minor ailments were treated. If anything at all serious was indicated, they were sent to one of the local hospitals by these examining doctors. The reception centers, as well as the local hospitals, were staffed on a rotating basis, new shifts every four hours. Each hospital set up its own method of sorting the casualties as they arrived. Those requiring admission were sent toward the accident rooms, x-ray, and wards on arrival. Those requiring outpatient care were sent to a large room where they were treated and later returned to the refugee centers. These refugee centers were set up in local high schools. Doctors made daily sick calls at these areas for the next week.

On Saturday, June 29, Dr. Hertell arrived with the offer of Red Cross aid for our medical teams (see page 1217). I would like to add that I have the highest regard and admiration for the work of the Red Cross. They did a fine job helping our people, and I am sure have done so in many other disasters. In spite of this, there are many people who for one reason or another are highly critical of the Red Cross. This seems to come to some extent from their overseas work in World War II. I think it is important for the Red Cross organization to know of this feeling, which is apparently generalized over the country. It is a serious thing, and I wish to do everything I can to overcome this. Dr. Hertell and his group did a fine job in helping us. When he talked with me on Saturday, I told him we would continue to man our aid stations and send doctors to the Red Cross shelters and refugee centers through the day on Sunday, but on Monday we would like the Red Cross to take over these functions so that we could get back to our private practice. This they did, and we mostly closed our medical services emergency care at that point.

Critique of Experience

In our critique of our actions resulting from the hurricane, we have several recommendations: First, the entire loss of life would have been avoidable with adequate warning and evacuation of people beforehand.

Second, the number of unidentified was disproportionately high. Some of this was due to entire families being wiped out. Some was due to late recovery of bodies after days out in the marsh. I think two steps would aid in identification. As I mentioned, 43% of the casualties were aged 17 or under. About two years ago our medical society auxiliary started fingerprinting all local school children and keeping these prints on file. This should be extended to the entire parish, and I would urge that it be done elsewhere. It would seem that many of the babies who were born in local hospitals might have been identified by their birth footprints. When this was attempted, it was found that the birth prints were so poorly made that they were not helpful in identification. Not one identification was established by this method.

Third, I feel that the supplies of the federal civil defense warehouses should be made available for such local disasters. Also, the medical society, the local civil defense, or the city should stockpile two federal civil defense 500-casualty aid kits. These supplies are listed in TM 11-1, Organization and Operation of Civil Defense Casualty Services, Part I, the First-Aid System, at a cost estimated at $1,500 per kit.

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Fourth, communications during an emergency are critical. During this operation, ours were very poor. In the city of Lake Charles most telephone service remained uninterrupted. The two hospitals were fortunate in this respect. We had no outside communication, however. Our communication with our aid teams was poor for 48 hours. To try and remedy this situation we have added a new man to our team, called the health services communications liaison officer. This man is a doctor and a radio amateur. I think he is going to be most helpful in getting us the proper communication set-up for another emergency.

Last, during this past emergency I set up my headquarters in Memorial Hospital. I did this primarily because the main civil defense headquarters seemed so crowded and it was difficult to get sufficient work room. Also, Memorial had two-way radio communication with civil defense headquarters. In another emergency, I would set up the health services headquarters in my office, which is large, has auxiliary power, and adequate telephone lines. After our experience, we still feel that our original premise that we could care for all types of local disasters, excluding enemy action, with local personnel, equipment, and hospitals, still stands.

HOSPITAL OPERATIONAL PREPAREDNESS

Joseph W. Hinsley, Lake Charles, La.

Preparedness for any type of disaster should be a continuous function in every hospital, as it is a definite responsibility of every hospital administrator to his community. In addition to planning for disasters occurring outside the hospital, the program should include fire prevention and safety measures within the institution. There are many problems that confront medical personnel in carrying out routine hospital care during a major disaster. It requires action on the part of physicians and hospital administrators to restore some degree of normalcy and to plan to work effectively under existing difficulties. It calls for the limiting of "Park Avenue" frills within established institutions and the standardizing of procedures and supplies for emergency hospitals and first-aid stations. It would be difficult to mention hospital accomplishments without sharing these honors with our physicians. We cannot describe hospital operational activity without recognizing the doctor as the motivating influence on all functions of the medical team.

During hurricane Audrey, I was playing the dual role of hospital administrator and health services coordinator of Calcasieu Parish Civil Defense, so my remarks may be influenced by either position. Audrey arrived in Louisiana at a time when the Calcasieu Parish Medical Society and the Calcasieu Parish Civil Defense were planning emergency disaster procedures for use on July 12, in connection with Operation Alert, 1957. On June 27, we were thrust into a situation wherein disaster became a reality instead of an exercise.

In presenting this subject, my remarks will first cover the need for hospital operational preparedness and second, a description of hospital plans in action during hurricane Audrey. In outlining a hospital plan from its origin to its use, it will be necessary to refer to my hospital in order to illustrate the problem. I might add that spreading our efforts over a 60-mile-long area during Audrey, in addition to maintaining a census beyond normal at our base hospital, was not included in our original planning but indicated how better prepared a hospital is to meet unforeseen emergencies if it has some basic plan for the care of mass casualties. The need for hospital preparedness will include comments on the nature of the preplanning at Lake Charles Memorial Hospital, showing the many items of additional equipment necessary, the importance of communications and transportation, plans for making maximum bed capacity available, and providing a reservoir of trained personnel.

Administrator, Lake Charles Memorial Hospital.

While describing the operation of the hospital during hurricane Audrey, I will trace the call for action and the trip to the devastated area, the setting up of the civil defense emergency hospital, the care and evacuation of patients at the scene of the disaster, and the care of evacuees at Lake Charles Memorial Hospital. This will clearly show our activity during the stress of disaster and I shall briefly analyze the compatibility of our planning with the actual operation. In addition, I would like to evaluate this experience as an aid in planning for a national disaster, showing the hospital's place in the survival plan after possible nuclear attack and the strain it will place on the entire medical structure.

Hospital Operational Preparedness

The plans of any hospital should include special training of the administrator or other hospital official. Hospital associations throughout the country are conducting institutes on disaster planning, fire prevention, and safety and have published many fine manuals on these subjects. The attitude of the hospital administrator toward civil defense or disaster planning is very important in the community, as many will follow his example, whether it be one of action or apathy. Personally, I availed myself of the administrative course with the staff college of the civil defense administration, the management of mass casualties course given at Brooke Army Medical Center, and I also had the privilege of attending Operation Rebound, at Houston (see *J. A. M. A.* **166**:785-787 [Feb. 15] 1957). Time will not permit a description of these courses, but I am deeply appreciative of having had the opportunity to attend and hope that my continued efforts along disaster planning will be a token of the respect I hold for those who planned and conducted these courses. Their untiring zeal indicated how dedicated they were to this life-saving, even nation-saving, service.

The plan of Lake Charles Memorial Hospital for disaster care began with the preparation of a manual, designed specifically for this hospital, which described the basic plan of operation for each type of disaster and gave explicit instructions to each department head under each classification. The plan included (1) the expansion of hospital service within our 100-bed hospital, (2) extension of our services into subsidiary hospital units, and (3) complete evacuation of the hospital. Execution of the second and third phases was not necessary during hurricane Audrey, although it is conceivable that had the destruction along the Louisiana coast

not been so violent and complete, we might have put phase two into operation. In coordination with civil defense, we had arranged for establishment of emergency hospitals in two school buildings, both within three city blocks of the hospital facility. The parish school board had made blueprints available to us and each room in the two buildings had been preassigned for some specific service during an emergency. Our over-all disaster plan took into account the interdependence of the medical and hospital functions with the civil defense services of rescue, transportation, police, welfare, engineering, communications, and supply. Although independently developed, our plan was integrated with community plans.

Our first attention in maintaining continuity of service had been directed toward providing emergency power to supply our needs in the event of public power failure. We had on hand five emergency generators, three of which we counted on to furnish 160 kw. to sustain our lighting and power equipment. One of these was a 35-kw. generator permanently mounted in the hospital to supply emergency lights, power for oxygen tents, and minor-powered equipment such as nurses call systems, paging system, telephone switchboard, our radio transmitters, and other items which could be plugged into the lighting circuit. Through a government surplus agency we obtained two 62.5-kw. generators to supply the major power demands of the hospital. There was a 15-kw. generator maintained exclusively for emergency use outside of the hospital. (We loaned this particular unit to the other local hospital during the hurricane.)

Arrangements for emergency water supply had been made with a local department store that had its own deep well, normally used for air-conditioning purposes only. Our fifth and smallest generator was a 2.5 kw. on standby to furnish electricity for the water project; however, this unit was adaptable for further emergency use in supplying electricity for a field x-ray machine or mobile radio equipment. As a matter of routine preparedness, we carried an inventory of food, linen, and medical supplies greater than projected normal requirement. We had in store items of strict emergency identification: 100 army-type cots, litters, and a stock of paper items (blankets, towels, dishes, and cups). In addition, we had custody of a 200-bed civil defense emergency hospital and had purchased a large van for transporting and storing the essential supplies of the unit. Only a few months before Audrey we had color-coded the 256 separate boxes of the unit to facilitate and expedite the setting up of this hospital under emergency conditions. We had displayed the hospital to the public at the annual meeting of the Louisiana Hospital Association held in Shreveport, La., during April, 1957.

Our radio service consisted of three stations: (1) an aeronautical advisory station, WKP6, tested regularly with intercom stations and through courtesy of members of the Air Force; (2) our "Mutual Aid" station, KKL-720 Zone 32, which connected up with all industrial plants, the fire department, police department, civil defense, weather bureau, and the Lake Charles Air Force Base; and (3) our emergency medical channel, Station KKS-407, with mobile transmitters located in emergency vehicles of the hospital.

Through our local civil defense, we had arranged for the immediate dispatch of 15 radio-controlled cabs and 40 civil defense policemen to the hospital in case of emergency. We had negotiated for helicopter ambulance and evacuation service with a helicopter service company that has 19 planes located one-half hour's flying time from Lake Charles. My hospital maintains its own radio-controlled heliport which is ordinarily utilized by helicopters bringing in patients injured or stricken ill while engaged in off-shore oil drilling activity in the Gulf of Mexico or the inaccessible marshlands. The heliport is equipped with landing lights, field lights, spotlights, and illuminated windsock. To make the maximum number of beds readily available within the limits of our 100-bed hospital, we summarized the "condition" sheets of the patients at eight-hour intervals as to the type of transportation needed for transfer, discharge, or evacuation.

To staff the hospital and extended facilities, we made plans for increasing our graduate nurses by 50%, not including the nurses working in doctors' offices and clinics, health centers, schools, industry, or the American Red Cross. We have a normal complement of 80 trained employees in our nursing department. When we went on a 40-hour week about three years ago, we hired 39 part-time employees, mostly married nurses who wished to work only two days each week but who could be called upon for relief or emergency scheduling. This contingent of trained professionals made up our reserve nursing corps. With the aid of Red Cross instructors, we had trained organized groups in first-aid, with the definite assignment as nurses' aides within the hospital's plan for emergency care.

The nursing department is responsible for the welfare and reassurance of regular patients, advance sterilization of extra packs, dressings, and instruments, replenishment of all supplies in the emergency room, as well as on each nursing unit, and the stocking of sufficient supplies and instruments on the first floor to furnish additional emergency rooms. Additional operating rooms were in our plan and consisted of the cystoscopy room and the treatment rooms on each floor.

The dietitian's plan included ordering an extra day's supply of milk and bread, preparing menus in advance that could be expanded or changed, based on the canned goods or frozen foods in store,

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and insuring that key food-service personnel were available for duty. This, generally, was our written program and the state of our preparedness on the day that radio bulletins began warning that the tropical storm Audrey was gathering intensity of hurricane proportion and was heading for the coasts of east Texas and southwest Louisiana.

Hospital Operational Preparedness During Hurricane Audrey

We began to divert our attention from a "mock" bombing attack to a potential hurricane on June 24, when we received the first news about Audrey. On June 26 we received from nearby Lake Charles Air Force Base Hospital, under its evacuation plan, the civilian dependents of air force personnel, six of whom were incubator babies. Our 100-bed hospital census now totaled 107 adults and children and 12 babies. Every weather bureau report from that time on was recorded on a tape recorder as it came over the radio network. The administrator and key personnel were kept constantly advised of these periodic reports. Each department fulfilled its advance responsibilities. Medical, surgical, and emergency teams were organized. Medical supply needs for each team were itemized and stocked in the team's area of operation. Step-by-step instructions were developed; responsibility was defined. Administrative procedures were worked out, and a triage section was planned.

When the weather report was received at 10 p. m. on the night of June 26, radio and television announcers gave assurance that the center of the storm would not reach Lake Charles until late the following night, so it was decided that employees not on the 3 to 11 shift could go home and complete their preparations the following morning. But three hours later, at 1 a. m. on June 27, the weather bureau report was revised, placing the storm much nearer the coast of Louisiana than was expected, after giving consideration to the reported forward speed of the storm. This message was relayed to the administrator, and all key personnel were assembled at the hospital by 3 a. m. to complete any preparations scheduled for later that morning, and all preestablished precautions were placed in effect.

A general inspection was made and all small equipment stored outside the building was moved inside and other equipment was securely anchored. The inside inspection began with the doors, windows, interior stairways, and hatchways on the roof and penthouse machine rooms. All corridors and exits were checked to make sure no obstruction remained from the preparation period. Cots were taken from storage and distributed to strategic points of the building. Supervisors briefed their employees on the disaster plan and of the location of all fire extinguishers on their present occupational assignment.

The "morning coffee" which precedes breakfast was served a little earlier this morning and every effort was made to assure patients of their safety. People in Lake Charles had been warned by radio announcers to seek shelter in public buildings and schools if they resided in lightly constructed homes, and 164 individuals drifted into our lobby for safety. All our "guests" were registered for information and identification purposes, and those with small children were sent to the nurses' classroom where blankets and mattresses were placed on the floor as the center of activity of each family group.

The winds increased to 105 mph and our chief concern was one of apprehension rather than action. Admissions were no higher than usual, with only 10 local people admitted as the results of injuries caused by the storm, but we did have an influx of expectant mothers. Winds began to diminish in the evening and most of the adult guests began to leave about 6 p. m., when the winds had subsided to 53 mph. The family groups waited about one hour longer. The administrative personnel, after being assured that the 3 to 11 crew had everything under control, began leaving for home at 8 p. m. Up to this time we had admitted 12 from the area of Cameron who, being cut off from communications, had no idea of the severity of the disaster.

Call for Action and Trip to Devastated Area

The real call for action originated with a radio announcement at 11:30 p. m. on June 27 from the only local radio station on the air, stating that civil defense was preparing to send the health services unit into the areas of Grand Chenier, Cameron, and Creole. I contacted civil defense headquarters and the director of medical services, Dr. Leonard Knapp (see page 1210). Civil defense officials told me to gather medical supplies for at least 1,000 casualties and prepare to leave for areas to the south that were harder hit than Lake Charles. Six army amphibious trucks from Alexandria, La., would be at Lake Charles Memorial Hospital by 4 a. m., June 28, to transport personnel and supplies to the stricken area by way of Creole, and cars would be there to transport part of the personnel to a Coast Guard cutter that would go direct to Cameron. Realizing that time would not permit my obtaining supplies from anywhere except my own hospital, I decided to take emergency supplies from Lake Charles Memorial Hospital and to also take the 200-bed civil defense emergency hospital into the disaster area.

These supplies, with doctors, nurses, and other hospital personnel assembled by the director of medical services, left at the scheduled departure hour. Roads were inundated, and for miles around only fragments of homes remained standing. The trip was delayed on several occasions while fallen wires and other debris blocking the path were re-

moved from the roadway by Army personnel. It was necessary to keep a constant lookout for low-hanging power lines. After one and one-half hours we made our first service stop for some people who had survived the storm in boats that had been washed ashore. First aid was administered and we proceeded in the six Army amphibious trucks to Creole which was about central in the devastated area. On reaching Creole, we looked for a building in which to set up our emergency hospital and to use as a supply center, but not a suitable building was standing, so we set our base hospital on the only high spot in the road with water surrounding us. From this point two Army vehicles, with nurses and a physician, were dispatched to Grand Chenier, and all other trucks were sent to Cameron. Before leaving, they radioed for helicopters and trucks to come as near the location of the hospital as possible and evacuate all persons from the area. The operation was chiefly one of first aid and evacuation, but about 7% were in serious condition. From this point on, our only communication system was the relaying of messages by incoming helicopters.

We divided our hospital area into three sections for operation. The first part was reserved for evacuation, and poles were chopped down to facilitate the landing of helicopters. The supplies were set up in the middle section and cots were spread out as far as possible. Boats unloaded their patients in the middle of this area and, after examination and treatment, patients were tagged for evacuation and any medicaments or injections given were indicated on the tags. Those more seriously in need of hospital care were marked for transfer to Lake Charles by helicopter and the remainder were sent in by motorboats to a point in the road to Lake Charles accessible by Army trucks. As many as five helicopters would be at the heliport of Lake Charles Memorial Hospital at one time. We examined, treated, and evacuated over 700 medical patients in less than eight hours in the Creole area with only about one-half of these patients needing further treatment. Of the 370 patients received during this eight-hour period at Lake Charles Memorial Hospital, more than 200 were received at the heliport and every one survived.

After the expedition left Lake Charles Memorial Hospital at 4 a. m. for the disaster area, all supervisory personnel were telephoned and they in turn notified their employees to report to work and most of them were on the job before 5:30 a. m. Patients who were able to be discharged were made aware of the emergency, their relatives were notified, and by 7 a. m. 60 patients had been transferred to their homes. Additional cots were set up in various rooms of the hospital, the conference room was converted into an emergency ward, and the main lobby was equipped as the triage section where patients were examined, sorted, and assigned. Emergency room record forms were used for processing all patients, with the examination, medication, and final disposition being indicated thereon. As outpatients were treated and discharged, they were transferred by ambulance to one of the refuge centers established in the city. This relieved congestion and confusion in the lobby and administrative wings. The processing of 370 patients in eight hours was a good day's work. In approaching an analysis of the effectiveness of our operation, I think that figure speaks for itself.

Compatibility of Planning with Actual Operation

With few exceptions, our operation was consistent with planning, and we experienced a minimum of confusion and disorganization. Our dietary department served 623 additional meals during this first day of evacuation. Their problems included the preparing of a second lunch for all employees when a large plate glass window crashed in the dining room, spoiling all the food on the steam tables. If one point in our preparation was more outstanding than others, it was the smooth operation of the triage section. The nursing personnel were amazed at the orderly operation of this department in a private general hospital under emergency conditions. This center was responsible for the continuous evaluation of the potential treatment that could be given and of the supplies available, and for the changing of category of patients from or to the delayed service group. It was the exponent of the medical service in planning the best for the most.

Having tested our plan in a natural disaster and making the necessary refinements in the program, the logical development is to consider its application in case of a nuclear invasion. Assuming there would be 16 million patients and only 1,500,000 hospital beds remaining, the problems of the physician and hospital administrator would be almost inconceivable—but this is another story. In closing, I would like to emphasize the medical relationships that prevailed during hurricane Audrey. When the Calcasieu Parish Medical Society voted not to charge the hurricane victims for their services, I was determined that nothing should happen to destroy the doctor-patient relationships established. On the bills for service to refugees at my hospital all laboratory and x-ray fees were cancelled, the doctors from these departments and the hospital each making his contribution so that the desire of the medical society to give 100% free service was realized. I appreciated the manner in which the American Red Cross cooperated in the payment of hospital bills—accepting responsibility for all those unable to pay, and they also paid for the supplies taken from my hospital and sent to Cameron and Creole, as well as the meals served to the refugees.

To me, hurricane Audrey brought out a manifestation of the hidden qualities in most of us. It was demonstrated by the donating of services, money, and materials. It was a characteristic shared by the medical profession whose donation of services and medical supplies was an outstanding gift to the hurricane victims. During this age when some folks talk of the decline of Western civilization, it is refreshing to learn from the research brochures of the National Academy of Science that the altruistic pattern displayed during hurricane Audrey is prevalent in all disaster areas of this country.

MEDICAL PREPAREDNESS FOR DISASTER

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The subject of medical preparedness in disaster is vital and timely, for the responsibility of the individual physician as well as organized medicine within the community is the care of the ill and injured, whether the disaster is caused by man-made devices or by the forces of nature. There is only one resource of competent organized medical assistance at the local level for any disaster—the county or parish medical society. At a recent meeting in Atlanta, the chairman of the medical preparedness committee of one of our southern state medical associations made the statement that the title "Civil Defense Administration" should be changed to "Natural Disaster Administration." Similar sentiments have been voiced and published by members of the medical profession in recent years. What is implied in these articles and pronouncements, of course, is that the federal government should assume the full responsibility in the field of natural disaster through the civil defense administration, and that private resources and concepts of self-help and neighbor-helping-neighbor are impractical and ineffective. Do we really want our government to assume the burdens of natural disaster in this nation? Certainly such suggestions from members of the medical profession, a profession which has consistently opposed government encroachment upon the lives and affairs of the American community, sound paradoxical to say the least.

There is no conflict or confusion concerning the roles of the Federal Civil Defense Administration and the Red Cross at the national level. Obviously, in a man-caused disaster, the problems would be of such magnitude that only the federal government could cope with them. The Federal Civil Defense Administration was established in 1951 as the government agency which will cope with such problems. As in previous wars, the Red Cross will again serve as a resource to the federal government to carry out such roles as are appropriate and yet maintain its special, unique organizational integrity to fulfill the special responsibility placed upon it by the Congress of the United States.

Southeastern Area Medical Officer, American Red Cross.

The American Red Cross has functioned as the nation's volunteer disaster relief agency since the Michigan forest fires in 1881. The organization was given an official mandate in this field by Act of Congress in 1905. The basic philosophy of the American Red Cross disaster relief program is predicated on the thesis that people want to do all that is within their power to help themselves to recover from the effects of disaster and thereby retain their independence and self-respect. The first responsibility is for the family unit, within its capacity, to meet as much of its own disaster-caused needs as possible. Then, the American people, through the Red Cross, bridge the gap between what the families need as a result of the disaster, and what they can do for themselves by providing supplementary assistance which will enable the family to regain self-sufficiency. In so doing, all existing resources, public and private, federal, state, and local, are utilized. In disaster rehabilitation, the Red Cross uses the techniques of family case work and the skills of an experienced disaster staff in accomplishing this purpose.

Congress, in authorizing federal assistance in major disasters, provided for the closest cooperation with the American National Red Cross. Public Law 875 spells out the essential difference between disaster relief provided by the Red Cross with voluntarily contributed funds, and that provided by agencies of the government operating with appropriated funds. The Red Cross and government together in natural disaster provide for meeting the needs of disaster-stricken communities. The task of the Red Cross is to help the individuals who need immediate shelter, food, clothing, and medical care, and to develop and implement a family rehabilitation plan to help disaster-affected individuals back to normal existence. It deals with human needs. The task of government is directed primarily to the restoration of public works, rebuilding bridges, repairing roads, and restoring other public property (table 1).

In the field of disaster relief then, the American National Red Cross has both a legal and moral mandate that it has neither the power, nor the right, to surrender. So far as we know, there is no thought or desire on the part of the responsible

officials of our government to create a "Natural Disaster Administration" as such. Through its first 75 years, the Red Cross participated in 6,000 disaster relief operations in this country, giving assistance at the cost of more than 200 million

Table 1.—*Interrelated Red Cross and Governmental Responsibilities in Disaster*

Red Cross Responsibility Relief of persons in need as result of disaster (financed by Red Cross from voluntary contributions)	Governmental Responsibility Protection of life, property, public health and welfare, and maintenance and repair of public property (financed by public agencies from tax funds)
Red Cross provides	Governmental agencies provide
A. Emergency assistance for disaster sufferers on mass care basis	A. Emergency community services
1. Food: canteen service and other facilities for feeding of homeless persons and volunteer workers	1. Police services within devastated zones and traffic controls, law, and order in the disaster area
2. Shelter: temporary shelter for numbers of persons made homeless; referral service for individual family lodging when available	2. Safeguards for public health and sanitation; i. e., water supply, sewage, facilities for the control and care of communicable diseases
3. Medical aid: first aid, nursing, and medical care to supplement local resources	3. Special police and fire protection for the disaster area and for shelters and relief stations
4. Clothing: distribution from emergency relief stations	4. Identification and care of the dead, including temporary morgues
B. Emergency services on individual family basis	5. Designation of hazardous buildings and areas
1. Welfare information services on survivors and on those injured, ill, hospitalized, or dead	B. Usual community welfare services for dependent persons
2. Emergency orders for food, clothing, rent, bedding, and similar essentials to enable families to maintain themselves	1. Institutional care for the aged, sick, orphaned, and other dependents
C. Rehabilitation of families	2. Public assistance grants to indigent persons; i. e., OAA, ADC, aid to the blind, vocational rehabilitation, general and home relief
1. Casework services	C. Restoration of community
2. Food, clothing, and other maintenance until normal sources of family support are restored	1. Repair of sewage and water systems and of streets and highways
3. Building and repair of owner-occupied homes	2. Removal of debris from public property
4. Essential household furnishings	3. Restoration of public transportation and communication facilities
5. Medical and nursing care	4. Repair of public buildings; i. e., schools, hospitals
6. Occupational supplies and equipment to restore family self-support	5. Salvage of unclaimed property

dollars. It should be emphasized that all Red Cross assistance is an outright gift of the American people, and is never repaid.

It must be emphasized that the vast majority of work on these operations was done by Red Cross volunteers without compensation. In addition, much material assistance was donated through 3,703 Red Cross chapters which serve every geographical subdivision in this nation.

Red Cross–Civil Defense in Hurricane Audrey

In hurricane Audrey, one finds a good example of what I have stated. Immediately upon learning that a hurricane threatened the Louisiana coast, the local chapters of the Red Cross and the local offices of civil defense for the parishes went into action in accordance with prearranged plans with utilization of all local resources. Rescue operations were undertaken by civil defense, utilizing resources from the armed forces, the National Guard, the Civil Air Patrol, and the Coast Guard. The Red Cross chapters immediately began preparing and opening shelters. Food and clothing for the evacuees became the responsibility of the Red Cross, as did the recruitment of additional nurses, the procurement of additional medical supplies, the setting up of first-aid stations in the area, and the feeding of the rescue workers themselves. Civil defense found itself faced with the problems of traffic control, communications, guarding against looting, and the enormous public health problems existing in the area.

In short, civil defense had to assist a parish government to get back on its feet. The Red Cross had to help the individual family to regain a productive place in society. Even within the past few weeks, Red Cross was still building homes, replacing destroyed furniture and clothing, and giving the families of Cameron, Creole, and Grand Chenier the things they needed to pick up the place of responsibility in the community they had lost last June. Civil defense was still working with the agencies of government to repair roads and bridges, rebuild schools, and restore public property in general.

Two Red Cross staff nurses were in Lake Charles when the disaster occurred. One of these worked with the chapter disaster committee in the early hours of the disaster in providing medical and nursing supplies and nursing personnel in shelters. The other worked with the medical and nursing teams evacuating the ill and injured out of the affected area. An additional nurse was sent into the Sabine Pass, Texas, area to assist with medical and nursing problems there.

Table 2.—*Some of the Major Disaster Relief Operations in Red Cross History*

Yr.	Disaster	Red Cross Expenditures
1906	San Francisco earthquake and fire	$ 3,100,000
1925	Missouri-Illinois-Indiana tornado	3,300,000
1926	Southern Florida hurricane	4,500,000
1927	Mississippi Valley flood	17,000,000
1930	Drought relief	11,100,000
1936	Spring floods	6,200,000
1937	Ohio-Mississippi Valley floods	25,600,000
1948	Central and Western Washington and Oregon floods	3,000,000
1951	Kansas-Missouri-Oklahoma-Illinois flood	14,400,000
1955	Eastern states floods	18,400,000
1955-56	Western states floods	8,500,000
1957	Eastern Kentucky, Virginia, West Virginia floods	5,900,000
1957	Southwestern Louisiana hurricane	2,700,000

I arrived in Lake Charles approximately 12 hours after the hurricane hit and immediately contacted Dr. Knapp and Mr. Hinsley (see pages 1210 and 1213). This was the beginning of daily contacts concerning the multitude of problems on medical and nursing coverage of shelters and first-aid stations, medical problems in isolated communities in the parish, additional nursing personnel, and additional medical supplies. I also had daily meet-

ings with the parish health officer. The Red Cross medical and nursing staff were able to give him assistance in inoculating the people in the stricken area against typhoid, as well as assistance on public health problems in isolated areas.

Mobile volunteer first-aid teams directed by staff first-aid men were stationed in all isolated areas during the emergency period.

Of course the emergency period is but a small part of a disaster operation in terms of monies

TABLE 3.—*Medical and Nursing Aid Subcommittee of Red Cross Chapter Disaster Preparedness Committee*

The medical and nursing aid subcommittee sees that disaster victims receive the medical and nursing care they need. It is recognized that individual patient care of the ill and injured is a function of local physicians and that the health protection and sanitation of the affected community are official responsibilities of the appropriate public health authorities. Red Cross medical and nursing services are provided to augment existing community resources to make the necessary care available.

a. **Subcommittee Organization.**—The subcommittee chairman is responsible for the general direction of Red Cross medical and nursing activities and the appointment of subcommittee members. Responsibility for enlisting a specific professional group to assist the subcommittee is delegated to the appropriate committee member by the subcommittee chairman. Suggested key membership of the subcommittee includes:

(1) Chairman, physician (appointed from chapter medical advisory committee)
(2) Nurse vice-chairman and alternate
(3) Health officer (or designated representative)
(4) First aid chairman
(5) Hospital administrator (or representative from hospital council)
(6) Dentist
(7) Pharmacist

b. **Duties (and Community Sources of Qualified Personnel and Support).**

In Disaster	For Preparedness	Sources of Qualified Personnel and Support
Evaluate needs for medical, nursing, and auxiliary personnel.	Evaluate potential needs for medical, nursing, and auxiliary personnel on basis of hazards reported by survey subcommittee.	ARC services: blood program, first aid, nurse's aide, home nursing, Gray Lady, nursing.
Establish and staff first-aid stations and infirmaries where needed.	Develop plan for establishing first-aid stations, including mobile units, and medical and nursing care in co-operation with shelter subcommittee.	Other community soures: professional nursing groups, official health agencies, civil defense organization, voluntary health agencies, National Foundation for Infantile Paralysis.
Determine needs and arrange for provision of emergency medical, nursing, and hospital supplies, including blood for disaster victims.	Ascertain availability of whole blood and blood derivatives and arrange for provision in disaster.	
Mobilize and assign medical, nursing, and auxiliary personnel to hospitals, shelters, health organizations, and for home visiting.	Develop plan with local professional groups and health agencies for assignment of available personnel. Outline steps for assignment of chapter-trained personnel.	
Review hospital, medical, and dental bills to determine whether fees are consistent with Red Cross policy.	Survey community medical and health resources, and maintain current lists of facilities (hospitals, infirmaries, nursing homes) and personnel available for assignment (physicians, dentists, nurses, technicians).	
Obtain supplementary vehicles from transportation subcommittee to move ill and injured, and assign personnel, when necessary, to assist.	Formulate understanding with local hospitals (or association) regarding basis of care for ill and injured in accordance with Red Cross policies.	
Supervise sanitary facilities in mass shelters, first aid, and feeding stations, and other Red Cross installations in co-operation with health department.	Ascertain existing community resources for transportation of ill and injured, and evaluate adequacy in disaster emergency.	
	Plan with health department for supervision of sanitary facilities in Red Cross installations.	
	Interpret the subcommittee's plans to professional and health groups in the community and provide necessary training.	

c. **Procedures When Disaster Strikes.**—The medical and nursing subcommittee is responsible for mobilizing and co-ordinating Red Cross medical and nursing activities to help meet immediate needs. First steps include:

(1) Establishing and staffing first aid stations
(2) Assigning medical and nursing personnel where needed, including shelters
(3) Securing information on hospitalized patients
(4) Providing emergency medical supplies, including whole blood and blood derivatives

Assistance may also include arranging for the services of trained volunteers such as volunteer nurse's aides and Gray Ladies in hospitals and in Red Cross emergency installations. When there has been heavy loss of life, it may be necessary to assign nurses and trained volunteers to morgues for helpful services to relatives arriving to identify and claim the dead.

d. **How To Get Organized.**

(1) The chairman meets with the chapter medical advisory committee (or medical society if no advisory committee has been appointed), the health officer, and representatives from local hospitals, dental, nursing, and druggist associations. The chairman appoints members of the subcommittee (nurse members are recommended by the nursing service committee).

The nurse vice chairman enlists support from the chapter nursing services committee and appropriate nurse representatives from professional nursing groups, public health nursing agencies, and institutions to assume responsibilities for specific activities. (See ARC 1640E, Handbook for Physicians and Nurses, Disaster Preparedness and Relief.)

(2) In cooperation with representatives from the interested health groups, review available resources and develop a plan of operation.
(3) The subcommittee members recruit qualified personnel and assign them to specific duties as shown in subparagraph b above.
(4) The chairman calls a meeting of the committee to review plans that have been made and to project additional plans for action when disaster strikes.
(5) A written plan of action is prepared and submitted to the disaster chairman. The plan should include a directory of sources for reserve personnel, medical supplies, and equipment, with a listing of:
  (a) Members of the subcommittee
  (b) Hospitals, showing location, bed capacity, and maximum expansion
  (c) Projected location of shelters and first aid stations
  (d) Ambulance facilities
  (e) Nearest Red Cross blood center and local blood-collection resources
  (f) Sources for obtaining medical and nursing supplies commonly required for first-aid stations and shelters
(6) When the plan has been approved by the disaster chairman, circulate copies among all members of the committee. Ask them to post or keep the copy in an accessible place.
(7) Reach advance understandings with official and voluntary health agencies, civil defense, hospitals, medical, dental, and nursing associations, and druggists for joint participation in disaster relief and for orientation and training. (See ARC 1640E, Handbook for Physicians and Nurses.)

Red Cross nurses were assigned to aid stations in Creole, Cameron, and Lake Charles, as well as in shelters from Abbeville, La., to Orange, Texas. In all, 16 American Red Cross national nursing personnel, and 350 Red Cross volunteer nurses served on this operation. (This latter group gave 3,000 volunteer hours or the equivalent of 4½ months of 24-hour duty during the first 2½ weeks.)

committed. In general, only 15% of the Red Cross disaster budget is spent on the emergency phase of an operation. The rehabilitation phase accounts for about 85% of a disaster budget. During the latter phase, Red Cross nurses were assigned throughout the area to work with the case workers. Every injured or ill person who applied for assistance was visited. As of this date, over $66,000

has been expended by the Red Cross for medical and nursing care in hurricane Audrey. The final medical and nursing costs will approximate $70,000.

Red Cross–Medical Society Joint Planning

The county medical society is the group that is literally on the "firing line" when a disaster strikes a community. Certainly, measures undertaken hurriedly under the pressures of a natural disaster cannot be fully effective or economical unless there has been good predisaster planning. Each person or group near the scene instinctively supplies the skill or resources they happen to have. But too frequently these helpful activities operate independently, and confusion, waste, and duplication result. These can be avoided only when there is a complete predisaster knowledge of resources available and an understanding among all individuals and community groups as to how these resources can best be applied in a disaster emergency. It is only prudent, therefore, that each county medical society develop its plan of preparedness jointly with the other segments of the community while there is time to reinforce spontaneous aid with organized effort and responsible leadership.

In each county in the nation there is a Red Cross chapter whose charter obligation it is to prepare to take care of the needs of individuals should disaster strike the community. In each county in the nation, a medical society exists, which has the health of the individual in the community as its basic obligation. The effectiveness of each, of course, depends upon the community leadership on the one hand and the individual members on the other. Something like a century and a half ago, Thomas Jefferson declared that "Nature has implanted in our breasts a love of others, a sense of duty to them, a moral instinct in short, which prompts us irresistibly to feel and succor their distresses."

Physicians can attest to this. It is the motivation behind a man taking up the study of medicine. It is the continuing motivation of the practice of medicine. The American Red Cross began 76 years ago as the means for the American public to express this instinct. Certainly the community chapter can provide the broad community basis for the concept of neighbor-helping-neighbor in its daily services. In organizing against a time of disaster, the Red Cross chapter should have a disaster preparedness plan to harness all existing and potential resources to aid families. Local government, whether or not it is coordinated by civil defense, must likewise be prepared for its greatly increased role of public responsibility when disaster strikes. If a community is to be properly prepared for disaster, it must have a community preparedness plan (1) that is current, (2) that interrelates the specific plans of local government and Red Cross, and (3) that utilizes properly and fully the skills and abilities of all organizations, such as the county medical society.

When the forces of nature kill, injure, and destroy, the county medical society automatically has a key role of responsibility. It should have disaster preparedness plans, but they should not be made separately. They should be an integrated part of the total community disaster plan. This is of prime importance if the individuals and families devastated by disaster are to receive prompt and efficient care.

I should like to propose for your consideration a plan for a medical disaster preparedness committee which we have found to be workable. First of all, your key membership should include (1) a chairman, a physician appointed by the county medical society; (2) a nurse vice-chairman, appointed by the local nursing association; (3) the health officer or delegated representative; (4) the Red Cross first aid chairman; (5) a hospital administrator, preferably a representative appointed by the hospital council; (6) a dentist, appointed by the county dental society; and (7) a pharmacist. Certainly this plan would fit even the smallest of communities and is the minimum essential for adequate medical preparedness.

Let me suggest that you contact your Red Cross chapter and your city government to see what planning has been done. Perhaps you can provide the spark your community needs to develop its disaster planning. Let me assure you that the full resources of the national Red Cross organization and its 76 years of experience in this field are available to you and your community for this planning.

SECOND ALCOHOLISM INSTITUTE

Some 200 physicians, nurses, and others concerned with treatment of alcoholics gathered at the state research hospital in Galesburg, Ill., Jan. 29, for the second A. M. A. Institute on Alcoholism. A forum comprised of Illinois Public Welfare Director Otto L. Bettag and members of the A. M. A. Committee on Alcoholism discussed sociology, pharmacology, psychotherapy, medical treatment, and a doctor's over-all role—as these factors relate to the alcoholic. Comments included:

Dr. Bettag: "How can we measure the loss in potential creativity and productivity, here in Illinois, attributable to an estimated 333,450 alcoholics? One is reluctant to point out that the care of alcoholic patients in our state mental hospitals is costing Illinois taxpayers approximately two million dollars a year. Alcoholism's greatest cost is the mounting mortgage of misery it places upon our society."

Dr. Selden D. Bacon, professor of sociology at Yale University (as he was unable to attend the session, his paper was read by Alfred Slicer, director of the Illinois Division of Alcoholism): "The fact that many unhappy, neurotic, or maladjusted persons use alcohol beverages and do not become alcoholics suggests that an etiology more specific than the commonly ascribed psychological anomaly or maladjustment must be sought."

Dr. Harold E. Himwich, research director of the hospital at Galesburg: "A mild degree of cortical depression (effected by alcohol) serves as the relief from the cares of the day and secures relaxation before dinner. It is not alcohol but the way that we use it that determines its value to us."

Dr. Jackson A. Smith, professor of neurology and psychiatry at the University of Nebraska College of Medicine: "Psychotherapy as applied to the chronic alcoholic is an attempt to encourage the patient to express anger and, thus, to prevent its accumulating and leading to increased tension, anxiety, and another bout."

Dr. Robert Fleming, staff psychiatrist at New England Deaconess Hospital: "The role of the doctor in alcoholism is to strive for total abstinence in the patient. There is no therapeutic middle ground."

Dr. Marvin A. Block, assistant clinical professor of medicine at the University of Buffalo, and chairman of the A. M. A. Committee: "In the chronic alcoholic, we are dealing not only with a sick individual but with that individual in relation to his environment. The family physician is the best case-finder of alcoholism. He has in the alcoholic a challenge from which he cannot retreat."

Referring to personal drinking habits as related in the autobiography of 84-year-old Sir Winston Churchill, Dr. Bettag asked his fellow panel members whether they considered Churchill an alcoholic. Dr. Block replied that only the reason for drinking, and not the amount of alcohol consumed, could determine this. Dr. Smith's wry response was: "It might take awhile, but alcohol will finally get Churchill."

The first A. M. A. Institute on Alcoholism was held last fall in San Francisco. It's next meeting probably will be held in a Southern state, in September or October, according to Dr. Block. The Illinois session was co-sponsored by the Illinois Department of Public Welfare, University of Illinois College of Medicine, Illinois State Medical Society, Knox County Medical Society, McDonough County Medical Society, Peoria Medical Society, Peoria Mental Hygiene Clinic, and the Galesburg Academy of Medicine.

NEW RADIO HEALTH SERIES

To give communities a monthly report on the newest and best in medicine, the American Medical Association is introducing its new radio transcription series—"Health Magazine of the Air"—which is based on current items from *Today's Health* magazine. The new 15-minute series features H. V. Kaltenborn, veteran newscaster, and Dr. W. W. Bauer, Director of the A. M. A. Bureau of Health Education. The programs are produced by the Marshall Organization, Inc., under the direction of the Bureau.

Seasonal health announcements—three 15-second; three 30-second; and two one-minute spots—will be presented on the reverse side of the platters. These spots will be given by popular movie personalities who contribute their time as a public service.

First shipment of the new transcriptions will be made to about 400 radio stations throughout the United States in February. The platters will be released about the fifth day of each month from February through December, 1958, for immediate broadcast. Although the present selection of stations has been based on those previously airing A. M. A. radio transcriptions, local medical societies may contact the Bureau of Health Education for further information regarding additional outlets.

CONFERENCE ON PERINATAL MORTALITY

The Committee on Maternal and Child Care of the Council on Medical Service will meet March 22-23 in Chicago. The second day of this meeting will be a joint conference with North Central area physicians interested in problems concerning perinatal mortality and morbidity. This will be the second regional meeting on this subject. Representatives of state and local medical society committees, state and local health departments, and individual hospitals from the following states have been invited: Illinois, Indiana, Iowa, Kansas, Kentucky, Michigan, Minnesota, Missouri, Nebraska, North and South Dakota, and Wisconsin. The Committee is working toward the development of a "Guide for Study of Perinatal Mortality and Morbidity" as an appropriate sequel to its 1957 publication, "Guide for Maternal Death Studies."

COUNCIL ON INDUSTRIAL HEALTH

Immunization, medical guidance, and health education—as they all relate to occupational activities—were among topics considered by the A. M. A. Council on Industrial Health, in Milwaukee, last Jan. 25. The meeting preceded a Council-sponsored Annual Congress on Industrial Health. Among other actions, the Council:

—Voted that its Committee on Industrial Health Defense, headed by Dr. Norvin C. Kiefer of New York City, work with the A. M. A. Committee on Civil Defense to develop a plan for immunization, particularly in emergencies.

—Recommended to the Board of Trustees that an *ad hoc* committee be established to prepare a guide for medical programs for construction proj-

ects. This guide would consider any special working conditions that require supplementation to the Council's already-established "Scope, Objectives and Functions of Occupational Health Programs."

—Heard a final report of its Committee on Health Education in Industry which, since last April 10, had been assigned the task of surveying industrial health education programs throughout the nation. Chairman Arthur K. Peterson reported that studies of state and community programs indicated that "since it would require millions of dollars to furnish health education material to tens of millions of workers, the Committee feels this problem is too large for the American Medical Association to conduct." Instead, he recommended that organized medicine pursue this function in cooperation with voluntary health associations, insurance and other private companies, and agencies at every level of government—all of which now make "a tremendous amount of health education materials available to industry."

MEETING ON THE AGED

A regional meeting of the A. M. A. Committee on Aging will be held March 29-30 in Birmingham, Ala. Representatives of the state medical associations of Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North and South Carolina, and Tennessee have been invited to attend the conference sponsored by the Council on Medical Service. This meeting will be similar to those held previously in Seattle, Dallas, and Philadelphia. Proceedings of some of these earlier meetings have been published and are available on request from the Council.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

POSTGRADUATE COURSES

Notice of the following postgraduate courses for physicians has not previously been published and is presented by the Council for information only:

The University of Washington School of Medicine, Seattle 5, will present a one-day 6-hour postgraduate course without fee on March 29, 1958, **Pathogenesis and Treatment of Edema and Hypertension.** Educational methods include lectures, panel discussions, and case presentation. Inquiries should be addressed to the Division of Postgraduate Medical Education of the school.

A three-day postgraduate course, **Clinical Physical Medicine,** has been scheduled for May 5-7 by the Office of Postgraduate Medical Education of the University of Colorado School of Medicine, Denver 20.

The University of Maryland Department of Zoology, College Park, Md., has scheduled the **Summer Institute of Acarology** for June 23-Aug. 1, 1958. This lecture and laboratory work course provides opportunity to study mites and ticks, with special emphasis on the transmission of diseases, for parasitologists, entomologists, and other advanced students in biology. The fee will be $49 for 3 weeks or $79 for 6 weeks.

An intermittent course for one and one-half hours each Thursday evening for three weeks on **Cancer Detection** will begin June 5, 1958, at the Memorial Center for Cancer and Allied Diseases, 444 E. 68th St., New York. The lecture and discussion period course is sponsored at no fee by the New York County Academy of General Practice. Inquiries should be addressed to Dr. Joseph A. Pincus, Registrar of the Academy, 140 W. 58th St., New York 19.

On June 20-21, 1958, a postgraduate course for physicians and coaches on **athletic injuries** will be offered in Eugene, Ore., with sponsorship by the University of Oregon Medical School and the Lane County Medical Society. The 2-day 14-hour lecture, demonstration, and question-period course, with use of visual aids, will take place in Room 102, Education Building, University of Oregon, Eugene, at a fee of $25., of which $5. is a nonrefundable advance registration fee that should accompany the application.

The American College of Physicians has scheduled a course, **Internal Medicine**, for full-time specialists, June 16-20 at the University of California School of Medicine, San Francisco. Inquiries or applications should be made to the Registrar, American College of Physicians, 4200 Pine St., Philadelphia 4.

A one-day postgraduate course, **Symposium on Diuretic and Antihypertensive Drugs,** is scheduled for March 28, 1958, at the University of Oregon Medical School, Portland, without charge to physicians attending.

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MEDICAL NEWS

CALIFORNIA

Symposium on Cerebral Palsy.—The 1958 Symposium on Cerebral Palsy will be held March 15 in Room 214 Medical Sciences Building, University of California Medical Center, San Francisco. Arranged by the Medical Advisory Board of the United Cerebral Palsy Association of San Francisco, in cooperation with Stanford University School of Medicine and University of California School of Medicine and Medical Extension, the symposium will be limited to 90 participants. Dr. H. Russell Meyers, professor of surgery, State University of Iowa, School of Medicine, Iowa City, and Chester A. Swinyard, medical director, Rehabilitation Center, University of Utah, School of Medicine, will be guest speakers. Dr. Meyers will discuss "Neurosurgical Measures in Cerebral Palsy," and Dr. Swinyard will speak on the "Neuroanatomic and Physiologic Basis of Cerebral Palsy." Information and application forms may be obtained from Dr. Seymour M. Farber, Head, Medical Extension, University of California Medical Center, San Francisco 22.

CONNECTICUT

Cancer Conference in Hartford.—The 11th annual Connecticut Cancer Conference for Physicians sponsored by the Connecticut State Medical Society, American Cancer Society, Connecticut Division, and the Connecticut State Department of Health, will be held March 19, 12:45 to 4:30 p. m., at the Hotel Statler, Hartford. Dr. Robert Shapiro, of the Hospital of St. Raphael, New Haven, will preside, and Dr. Donald A. Bristoll, president, American Cancer Society, Connecticut Division, will open the program. "Rectal Bleeding," a symposium, will be moderated by Dr. William A. Meissner, assistant clinical professor of pathology, Harvard Medical School, Boston, and will consider medical, radiologic, pathologic, and surgical aspects. Speakers include Drs. Franz J. Ingelfinger, associate professor of medicine, Boston University School of Medicine; Robert D. Moreton, Fort Worth, Texas, clinical associate professor radiology, University of Texas School of Medicine; and William C. Bernstein, clinical associate professor of surgery (proctology), University of Minnesota Medical School, Minneapolis. An open forum will be conducted following the symposium. Dr. Shapiro will present the concluding summary. Members of the American Academy of General Practice may receive postgraduate credit for attendance. For information write the Connecticut State Medical Society, 160 St. Ronan St., New Haven 11, Conn.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

DISTRICT OF COLUMBIA

Dedicate Washington Hospital Center.—The Washington Hospital Center was formally dedicated Dec. 1 and will be opened March 10. Built on the southwest corner of the Soldiers Home grounds, it is a voluntary, nonprofit community hospital which represents the merger of three voluntary hospitals: the Central Dispensary and Emergency Hospital, the Episcopal Eye, Ear and Throat Hospital, and the Garfield Memorial Hospital. The center was built under an act of Congress, approved Aug. 7, 1946, "to provide for the establishment of a modern, adequate and efficient hospital center in the District of Columbia." The three hospitals received $21,700,000 to complete the center, subsequently increased by $1,710,000. On 46 acres of land, the hospital will contain 800 patient beds and will be completely air-conditioned. It has a gross area of 788,000 square feet and is planned for medical and surgical cases, maternity cases, and cases of short-term mental illness. It has a "completely equipped" emergency department and an outpatient department designed to treat 400 patients a day. In connection with the hospital is a School of Nursing to train a maximum of 300 student nurses at one time. Other teaching programs planned for the hospital center are schools for laboratory technicians, x-ray technicians, and practical training for medical secretaries. Features of the new hospital are electrically operated beds, a central sterilizing and supply suite, a radioisotope laboratory, a virology

The recently dedicated Washington (D. C.) Hospital Center.

laboratory, biological research area, blood bank, and "complete facilities" for the diagnosis and treatment of patients with visual and hearing defects. Dr. Warwick T. Brown is the hospital center administrator.

ILLINOIS

Chicago

Medical History Lectures.—The Society of Medical History of Chicago will meet in an open session at the Institute of Medicine March 12, 8:00 p. m. Dr. André Barbeau, department of medicine (neurology), University of Chicago, will present "History of Involuntary Movement." Dr. Joseph H. Kiefer, head, division of urology, University of Illinois, will speak on "Uroscopy—The Clinical Laboratory of the Past." Information may be obtained from Dr. Leo M. Zimmerman, Secretary, Society of Medical History of Chicago, 55 E. Washington St., Chicago 2.

Diabetes Study Program.—A training program for the study and treatment of diabetes is currently underway at Chicago Medical School under the direction of Dr. Piero P. Foa, professor of physiology. The program has been made possible by a grant of $10,622 from the U. S. Public Health Service. It is for a five-year term and includes a salary for the doctor in training. Dr. Giuseppe D'Amico, an internist and member of the staff of the department of medicine of the University of Milan is taking the special work. In 1956 he was awarded the "S. Pellegrino Fellowship in Medicine" and last year passed his Board of Internal Medicine examination.

Dustfall in Chicago.—The Armour Research Foundation of the Illinois Institute of Technology maintains some 25 stations throughout the city for the determination of the amount and chemical analysis of the dustfall. In its report for December, 1957, the average total dustfall at these stations, including the Loop, was 66.1 tons per square mile per month of 30 days and of this amount 37.7 tons were water insoluble constituents and 28.4 tons water soluble constituents. "The Loop average" total dustfall was 249.9 tons per square mile. The least amount of dustfall at any of these stations was 24.7 tons per square mile at a station in a far northwestern section of the city.

Conference on Alcoholism.—An all-day conference on alcoholism in industry will be held March 11 at the La Salle Hotel. The sessions, aimed at presenting specific information on how the incidence of alcoholism in industry can be reduced, are sponsored by the Chicago Committee on Alcoholism and the Chicago Association of Commerce and Industry. The theme will be "Saving Men and Money: How Industry Profits from Helping the Industrial Alcoholic." Industrial executives and a national representative of the AFL-CIO will participate. The morning conference session will present current information about treatment, with Dr. Melvin M. Chertack, clinic consultant, Chicago Committee on Alcoholism, speaking on "Medical Aspects of Treating the Alcoholic," and Dr. Patrick L. Israel, psychiatric director of the clinic for alcoholics operated by the committee, discussing "Psychiatric Aspects of Treatment." In the afternoon, Arnold J. Kuhn, Ph.D., executive director of the committee, will discuss ways in which this organization can aid companies in developing their programs. For information and reservations write the Chicago Committee on Alcoholism, 46 E. Superior St., Chicago 11.

LOUISIANA

Dr. DeBakey to Give Annual Matas Lecture.—The 11th annual Rudolph Matas Lecture, sponsored by the Beta Iota Chapter of Nu Sigma Nu at Tulane School of Medicine, will be delivered March 14, 4 p. m., in the Hutchinson Memorial Auditorium of the Medical School by Dr. Michael E. DeBakey, chairman, department of surgery, Baylor University College of Medicine, Houston. Dr. DeBakey's topic is "Changing Concepts in the Surgery of Aortic and Arterial Diseases."

MASSACHUSETTS

Annual Dunham Lectures.—The 1958 Dunham Lectures will be delivered at the Harvard Medical School, Boston, by Dr. Joseph Stanley Mitchell, regius professor of physic, University of Cambridge, and director, Radiotherapeutic Centre in Addenbrooke's Hospital, Cambridge, England, on March 10-13. Dr. Mitchell's general topic will be "Studies in Radiotherapeutics." Each lecture will begin at 5 p. m., scheduled as follows:

March 10—"Mechanisms of the Therapeutic Actions of Ionizing Radiations."
March 12—"Laboratory and Clinical Investigations of Radio-Sensitizers."
March 13—"Some Investigations of Practical Interest."

The lectureship honors the memory of Dr. Edward K. Dunham, a graduate of the Harvard Medical School in 1886. Its purpose is the promotion of "the bonds of fellowship and understanding between students and investigators in this and foreign countries." Lecturers are selected from investigators and teachers in the medical sciences.

Alumni Dinner Meeting.—The Tufts Medical Alumni Association will hold its annual dinner meeting March 26, 6:30 p. m., at the Somerset Hotel, Boston. The guest speaker will be Gilbert Cant, medicine editor of *Time* magazine, who will talk on the current changes in the relationship between the medical profession and the lay press, and the im-

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pact of these changes on patient-doctor relationships. The 25-year class, M'33, will hold its reunion and Dr. Joseph B. Kirsner, M'33, professor of medicine at the University of Chicago, will speak for the class. President Nils Y. Wessell, Ph.D., of Tufts University, and Dr. Joseph M. Hayman Jr., dean, Tufts Medical School, will make reports. For information write Dr. Harry Blotner, Tufts University School of Medicine, 136 Harrison Ave., Boston 11.

Personal.—Dr. James L. Tullis, Brookline, associate director of the Protein Foundation, Inc., has received a plaque for "outstanding glycerine research in 1957" from the Glycerine Producers Association. Dr. Tullis, who also received a cash award of $1,000, developed "a practical method for the long-term preservation of red blood cells at temperatures of −80° C and −120° C, using a 40% glycerine solution."—Dr. F. Floyd Mussells, executive director, Philadelphia General Hospital, has been appointed director of Peter Bent Brigham Hospital, Boston, and will assume his new duties on June 15. Dr. Mussells succeeds Dr. Norbert A. Wilhelm, who retired last June following 25 years with the hospital. Dr. Victoria L. M. Cass, associate director, is serving as acting director during the interim.—Dr. Martha M. Eliot, chairman, department of maternal and child health, Harvard School of Public Health, Boston, received an honorary doctor of science degree from Wayne State University, Detroit, Jan. 28.

MONTANA

Rehabilitation Association Organized.—The Montana Association for Rehabilitation was organized in Helena during January "to foster rehabilitation activities in Montana." Its membership is composed of interested laymen and professional persons concerned with rehabilitation problems. Dr. Howard N. Clemmons, Butte, was named president at the organizational meeting; Dr. Jess T. Schwidde, Billings, president-elect, Allen Myers, Billings, vice-president; Jack C. Carver, Helena, secretary; and Anna T. Beckwith, Helena, treasurer. Drs. John K. Colman, Butte, and Louis W. Allard, Billings, were named directors-at-large.

NEBRASKA

Annual Regional Meeting of Physicians.—The 12th annual regional meeting for Nebraska of the American College of Physicians will be held March 15 at the Cornhusker Hotel, Lincoln. Dr. Richard A. Kern, president of the college, Philadelphia, will be guest speaker at the banquet, presenting "Personal Observations in the Near and Middle East." The Nebraska Heart Association will present their scientific program in the morning starting at 9 a. m. Sessions in the afternoon will include the following:

Pain in the Neck and Shoulder, Dr. Harold N. Neu, professor of medicine, Creighton University School of Medicine, Omaha.

Cardiac Calcifications, Dr. Clarence K. Elliott, clinical assistant professor of medicine, University of Nebraska College of Medicine, Omaha.

Agammaglobulinemia, Hodgkins Disease and Hypersplenism, Dr. Robert L. Grissom, professsor of medicine, and Dr. Peyton T. Pratt, assistant professor of medicine, University of Nebraska College of Medicine.

Practical Tests of Pulmonary Function, Dr. Jerome Ritter, clinical associate professor of medicine, University of Nebraska College of Medicine.

Management of Cardiac Arrhythmias, Dr. Otto A. Wurl, assistant professor of medicine, Creighton University School of Medicine.

Isotopes as Diagnostic Aids, Dr. Richard E. Ogborn, director, Isotope Laboratory, Veterans Administration Hospital, Omaha.

For information write the American College of Physicians, 4200 Pine St., Philadelphia 4.

NEW JERSEY

Fund for Pharmacology Department at Seton Hall.—A contribution of $100,000 by Merck & Co., Rahway, to help found the Seton Hall College of Medicine and Dentistry has been announced. The gift was designated to provide facilities and equipment for the laboratories and offices of the pharmacology department. This gift is a contribution to the $9,700,000 Founders' Fund campaign to cover the cost of reconstructing and equipping facilities for New Jersey's first college of medicine and dentistry. Of this total, $5,300,000 will be used to pay for the equipment purchased and the renovations made at the Jersey City Medical Center site. The remainder will be used to maintain the new medical and dental school until the first class graduates in 1960. About $3,000,000 has already been raised toward the Founders' Fund goal.

Personal.—Dr. Joseph H. Fobes, Montclair, has been appointed part-time supervisor of medical education at the Harrison S. Martland Medical Center, Newark. His duties are to procure applicants for training as interns and residents and to organize a teaching program for them. He is also part-time director of the department of graduate surgical training at the New York Medical College, Flower and Fifth Avenue Hospitals, New York City.—The council of the American Pharmaceutical Association has elected Dr. Charles L. Brown, dean of the College of Medicine, Seton Hall College of Medicine and Dentistry, Jersey City, as a member of the Committee on National Formularly for a five-year term, succeeding Dr. Harvey B. Haag, who has been a member for 15 years and who asked to be relieved of this assignment.—Dr. John J. Thorpe, of Red Bank, has been appointed associate medical director of Esso Standard Oil Company.

NEW YORK

New York City

Schoenbach Memorial Lecture.—The sixth annual Emanuel B. Schoenbach Memorial Lecture will be delivered in the solarium of the Maimonides Hospital of Brooklyn April 24, 4:30 p. m. The guest speaker, Dr. Lewis Thomas, chairman, department of pathology, New York University College of Medicine, will talk on "Role of Hypersensitivity in Tissue Damage and Disease."

Establish Division of Neuromuscular Diseases.—New York University–Bellevue Medical Center and the national headquarters of Sister Elizabeth Kenny Foundation have joined forces to initiate a program for the investigation, treatment, and rehabilitation of Parkinsonism and related neuromuscular disorders. A division of neuromuscular diseases and a professorship of research surgery in the department of surgery at the University Post-Graduate Medical School have been established to carry out the program through a pledge of $1,250,000 from the Sister Elizabeth Kenny Foundation and its subsidiary, the American Rehabilitation Foundation. Dr. Irving S. Cooper will be the first incumbent of the professorship and director of the division. The chair will be supported by $250,000 of the total grant. The new division will be for the investigation, treatment, and rehabilitation of hyperkinetic diseases and related neuromuscular disorders. A sum of $1,000,000 will provide for construction of the physical facilities of this division in the 19-story general hospital whose construction is scheduled to begin early in 1959 at the Medical Center. Active consultants to the division will be Dr. Howard A. Rusk, chairman, department of physical medicine and rehabilitation; Dr. Walter A. L. Thompson, chairman, department of orthopedic surgery; and Dr. S. Bernard Wortis, chairman, departments of psychiatry and neurology. It is the intent of the grant to provide an interdisciplinary attack on neuromuscular diseases in which investigating teams from several departments will cooperate to further the center's knowledge of these diseases and of their treatment.

OHIO

Plan New Rehabilitation Center.—The Ohio State University Board of Trustees has announced that the new Ohio Rehabilitation Center, for which Ohio legislative appropriations total $1,015,000, will be located adjacent to the east boundary of university property near Perry Street and north of Eighth Avenue extended. Federal funds, which include Hill–Burton money and National Institute of Health grants for research facilities, bring the amount available for the new structure to about $1,250,000. The rehabilitation program, which has been housed in the Health Center since its creation in October, 1952, now occupies space in the Ohio Tuberculosis Hospital. The new center will permit increased service to severely disabled persons and provide an expanded program of education and research in cooperation with the university. A three-member board of control directs the rehabilitation program. Members are president Novice G. Fawcett of Ohio State, the state health director, Dr. Ralph E. Dwork, and the public representative on the State Industrial Commission, Mr. J. Maynard Dickerson. Dr. Ralph E. Worden is the medical director.

PENNSYLVANIA

Dr. Crabtree Succeeds Dr. Parran As Dean.—Dr. James A. Crabtree, head, department of public health service, has been appointed dean of the Graduate School of Public Health, University of Pittsburgh, succeeding Dr. Thomas Parran, who in 1948 organized the graduate school and now becomes director of the Avalon Foundation in New York. From 1938 until he came to Pittsburgh in 1949, Dr. Crabtree served with the U. S. Public Health Service, initially as an epidemiologist in the National Cancer Institute, and subsequently as executive assistant to the Surgeon General.

Philadelphia

University News.—The Kappa Pi Chapter of the Phi Delta Epsilon Fraternity will hold it's annual Bernard Comroe Memorial Lecture on March 21 at the University of Pennsylvania Medical School. The speaker will be Dr. Howard A. Rusk, of New York City, and his topic will be "Health for Peace."

Postgraduate Institute and Convention.—The 22nd annual Postgraduate Institute of the Philadelphia County Medical Society will be held March 18-21 at the Bellevue–Stratford Hotel. Two panel discussions are planned: "Recent Advances in the Treatment of Diabetes with Oral Medication," moderated by Dr. Garfield G. Duncan, and "Status of Poliomyelitis Vaccine" moderated by Dr. Joseph Stokes Jr. The program includes the following papers by guest speakers:

The Malabsorption Syndrome, Dr. David Adlersberg, New York City. Advances in Nutrition as Applied to the Practice of Medicine, Dr. William H. Sebrell Jr., New York City.

Evaluation of Renal Biopsy, Dr. Alvin E. Parrish, Washington, D. C.

Mechanism of Vascular Headache, Dr. Harold G. Wolff, New York City.

Problem of the Medical Management of Vascular Headache, Dr. Bayard T. Horton, Rochester, Minn.

Dr. Herbert E. Holling, London, England, will present "Physiology and Anatomy" the afternoon of March 18. Discussions will follow the formal presentations, and a clinical pathological conference will be held March 20. The meeting is approved for credit by the American Academy of General Practice. Registration fee is $10 for non-

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members of the society. For information write Dr. Charles W. Wirts, Director, 301 S. 21st St., Philadelphia 3.

Workshop in Kinesics.—Psycho-linguistics and the new field of kinesics will be the subject of a two-and-a-half-day workship, sponsored by the department of psychiatry at the Temple University Medical Center, March 20-22. The program, which will be conducted by Ray L. Birdwhistle, Ph.D., and Henry L. Smith Jr., Ph. D., of the University of Buffalo, is open to clinicians, researchers, teachers, and allied personnel in the mental health field. Interested registrants should apply to Dr. Max Katz at the Temple University Medical Center. Dr. Birdwhistle, founder of kinesics, the study of gesture and motion, has been associate professor of anthropology at the University of Buffalo since September, 1956. He also teaches regularly at the University of Pittsburgh and serves as a consultant in the research program at Temple University Medical Center. Dr. Smith is professor of linguistics and English, and chairman of the department of anthropology and linguistics at the University of Buffalo.

SOUTH CAROLINA

Dr. Lynch Honored.—Dr. Kenneth M. Lynch, president of the Medical College of South Carolina, Charleston, has received the Southern Medical Association's Distinguished Service Award. Dr. Lynch came to Charleston in 1913 as professor of pathology at the Medical College and pathologist for Roper Hospital. He became vice-dean of the college in 1936, dean in 1944, and president in 1949. He has been awarded the Gold Medal and Research Medal of the American and Southern medical associations. Offices he has held include secretary of the Pan-American Medical College; president, American Society of Clinical Pathologists; president, American Society of Tropical Medicine and Hygiene; and vice-president of the American Medical Association, as well as the presidency of the South Carolina Medical Association.

TEXAS

Annual Panhandle District Meeting.—The annual meeting of the Panhandle District Medical Society (36 counties) will be held in Amarillo March 22. Dr. Joseph B. Kirsner, professor of medicine, University of Chicago School of Medicine, will moderate a panel discussion on functional problems of the colon. Other speakers are: Dr. Ben J. Wilson, professor of medicine, Southwestern Medical School, Dallas; Dr. Emil G. Holmstrom, chairman, department of obstetrics and gynecology, University of Utah; Dr. Frank E. Whitacre, chairman, department of obstetrics and gynecology, Vanderbilt; Dr. Walter P. Anthony Jr., otolaryngologist from Fort Worth; and Dr. John L. Matthews, professor of ophthalmology, University of Texas Medical School, Galveston. There will be a social hour in the evening followed by a banquet and entertainment. On March 23 there will be a golf tournament at the Amarillo Country Club. For information write the Panhandle District Medical Society, Box 693, Amarillo, Texas.

GENERAL

Tuberculosis in the U. S.—The National Tuberculosis Association reports that there are 55 million people in the United States who have been infected with the tuberculosis germ and may or may not come down with an active case of the disease. Reportedly, the statistical odds are that 2,750,000 of them will break down with active tuberculosis sometime during their lives. Presently, about 80,000 new cases of tuberculosis are reported annually, although the death rate from the disease reached its all-time low in 1956: 8 deaths for every 100,000 persons in the U. S.

Repeat Telecast of "Hemo the Magnificent."—The Bell System Science Series TV program on blood and its circulation, "Hemo the Magnificent," will be shown again the afternoon of March 16, over the NBC network. The hour-long program has three principal sections: (1) construction and functions of the heart, lungs, and digestive organs in the circulation of the blood; (2) functions of the arteries, capillaries, and veins; (3) priorities of blood flow to the cells of the brain, muscles, and digestive system. Dr. Maurice Visscher, professor of physiology, University of Minnesota Medical School, Minneapolis, served as principal advisor on the production of the program. First shown on television in March, 1957, it has been shown to more than three million people in group showings in the past year.

Meeting on Facial Plastic Surgery.—A combined meeting of the American Society of Facial Plastic Surgery and the department of otolaryngology, Ohio Health Center, Ohio State University, will be held March 10-11 in Columbus, Ohio. Guest of honor will be Dr. Irving B. Goldman, of New York City, who will lecture the afternoon of March 10 and present a motion picture on "Rhinoplastic Surgery," that evening. Surgical sessions will include two rhinoplasty operations and a Goldman septum operation. Dr. Edward W. Harris, chairman, department of otolaryngology at the university, will address the meeting March 10. Discussion periods will follow surgery in each case. A tour of the Ohio Health Center will conclude the meeting. For information write the Secretary, American Society of Facial Plastic Surgery, 123 E. 83rd St., New York 28.

Tri-State Tuberculosis Conference.—The sixth annual Tri-State Tuberculosis Case Conference will be held at the Roanoke Hotel in Roanoke, Va., March 16-18. The conference is sponsored by the Trudeau societies of West Virginia, Virginia, and North Carolina, together with the Virginia Department of Health. Dr. Carl Muschenheim, of New York City, will open the meeting March 16, 8 p. m., as guest speaker. Cases will be presented by the Veterans Administration Hospitals at Martinsburg, W. Va., and Oteen, N. C., and the Grandy Sanatorium, Norfolk, Va. Diagnostic problem cases will be presented March 18, with Dr. Thomas B. Barnett, of Chapel Hill, N. C., as the speaker. Dr. Theodore L. Badger, of Boston, president, American Trudeau Society, will be the moderator. The registration fee ($5) will be payable at the time of registration in Roanoke.

Medico-Legal Symposium on Back Injuries.—The American Board of Legal Medicine will hold a symposium luncheon on the "Medical-Legal Aspects of Back and Neck Injuries" in the Hotel Sheraton Astor, Times Square, New York City, at noon, March 19. The following are panel members: (physicians) Drs. Reuben Leass, assistant orthopedic surgeon, Queens General Hospital, Jamaica, N. Y.; Harold Lefkoe, orthopedist, Philadelphia; Samuel D. Critides, neurosurgeon, New York City; Louis J. Gelber, radiologist, New York City; (lawyers) Mr. Joseph Dean Edwards, New York City, and Mr. Maxwell M. Boorbaum, secretary, American Board of Legal Medicine. Judge of the symposium will be Justice John L. Flynn, of the New York Supreme Court, and the moderator of the symposium will be Dr. Alfred Koerner, president, American Board of Legal Medicine. Reservations ($6) may be made by calling in New York CHickering 4-6377 or by writing the American Board of Legal Medicine, 1501 Broadway, New York 36.

Pan-American Medical Women's Alliance.—The sixth congress of the Pan-American Medical Women's Alliance will be held in Miami, Fla., April 14-17, with headquarters at the Hotel McAllister. Women physicians of the United States and Canada are invited to become members and attend the congresses, which are held every two years alternately in North and South America. Delegates are expected to represent the medical women of most of the Latin-American Republics. The scientific program is translated into Spanish and English and deals with medical problems of mutual interest. Two post-congress trips are being planned; one is to the Caribbean area, where some of the member groups will be visited. The other is to Washington, D. C., where the hospitality of the Pan-American Union and the various Latin-American organizations is being offered. The Latin American Music Festival also is being held in Washington at this time. For information write Dr. Hilla Sheriff, Publicity Chairman, Division of Maternal and Child Health, S. C. State Board of Health, Columbia 1, S. C.

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MEDICAL EDUCATION
WEEK ···· April 20-26

Fellowships in Infant and Child Development.—Fellowships in developmental diagnosis are available at the Clinic of Child Development, which is sponsored jointly by the department of pediatrics, Ohio State University College of Medicine, Columbus, the Children's Hospital of Columbus, Ohio, and the Ohio State Department of Mental Hygiene and Correction. The clinic is concerned with the evaluation of neurologic status and maturity level in children in the preschool period suspected of having deviations in development. The majority of the children have neuropsychiatric disabilities which are organic in nature. In addition to diagnostic evaluation, guidance in the management of problems and help in securing the necessary medical and community services are provided. Fellowships are open to pediatricians, or psychiatrists who are board eligible. They are for a period of one year, beginning July 1 with one position each six months available, and carry a stipend of $5,000. Physicians who are trained will have opportunities to engage in research projects designed to elucidate the etiologies of the neuropsychiatric disabilities of childhood and to enter into the teaching program. Address inquiries to Dr. Hilda R. Knobloch, Director of the Clinic of Child Development, at the Children's Hospital, 561 S. 17th St., Columbus 5, Ohio.

Last Year's Catastrophes.—Natural disasters were responsible for more than a third of the deaths in catastrophes—accidents in which five or more persons died—during 1957, it is reported by statisticians of the Metropolitan Life Insurance Company. Catastrophe deaths in the U. S. totaled almost 1,700 during the year, or about 400 more than in 1956. The increase is largely a reflection of the unusually heavy loss of life in Hurricane Audrey, which caused about 350 known deaths in early June—most of them in Cameron, La. All five of the major catastrophes (those which caused at least 25 deaths) occurred in the first six months of the year. In addition to the hurricane, the others were:

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the fire which destroyed a home for the aged at Warrenton, Mo., on Feb. 17, causing 72 deaths; the May 20 tornado which struck the Kansas City area, killing 39; a gas explosion which killed 37 in a coal mine near Bishop, Va., on Feb. 4; and the March blizzard which killed 29 in the Great Plains states. Because of the heavy toll in the hurricane, the loss of life in natural disasters was the highest in nearly 20 years. Catastrophes involving motor vehicle mishaps and fires and explosions also took higher death tolls than in 1956. On the other hand, fatalities in civil and military aviation and railroad transportation were lower in 1957 than in 1956. The loss of life in water transportation was about the same.

Forum for Foreign Exchange Doctors.—The seventh annual forum, under the auspices of the Ventnor Foundation, on "The Dynamics of Democracy" was held in Atlantic City, N. J., Feb. 8-9. The forum is part of an exchange program, sponsored by the foundation, in which recent graduates of German and Austrian medical schools are brought to the United States for a year's work. The purpose of the program is to give these doctors "an opportunity to experience a discipline of medicine and a way of life different from that in their homeland as a means of waging peace through better mutual understanding." Fifty-one German and Austrian exchangees attended the forum. Two other similar groups also attended as guests of the foundation: One, a group of 12 French doctors working in the U. S. on an exchange program under the auspices of the Unitarian Service Committee; the other, a group of 28 foreign fellows under the direction of Dr. Howard A. Rusk, studying at the Institute of Physical Medicine and Rehabilitation of the New York University–Bellevue Medical Center. The Ventnor Foundation Exchange Program is carried on with the cooperation of the State Department but is operated entirely by private citizen effort and supported privately by contributions of the cooperating hospitals and individuals. Participants in the program included Dr. Isidor S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania, and president of the Ventnor Foundation, and Dr. Rusk.

National Health Forum in Philadelphia.—The 1958 National Health Forum, sponsored by the National Health Council in behalf of 63 member organizations, will be held March 18-20 at the Sheraton Hotel, Philadelphia. Principal speakers will be Governor Robert B. Meyner of New Jersey, who will address a dinner session March 18, and Luther H. Gulick, Ph.D., president, Institute of Public Administration, New York City, who will speak at a luncheon March 19. The forum will focus on trends in population change and movement and the impact on governmental structures, community organizations, and family life. Representatives of selected large and small cities will present case histories of urban sprawl and action taken by state, federal, and local agencies to cope with resultant problems. Specific areas to be discussed include community planning of hospitals and related services; cooperation between official and voluntary agencies in community research; effects of urban sprawl on local health department programs; special problems of private professional practice in cities and suburbs; new problems of voluntary health associations; mental and social health and environmental industrial health. Planned in conjunction with the forum are the 10th annual meeting of the National Advisory Committee on Local Health Departments and the annual meeting of delegates to the National Health Council. Information on registration is available from National Health Council Headquarters, 1790 Broadway, New York 19.

FOREIGN

Symposium on Freezing and Drying.—The Institute of Biology, England, is arranging a Symposium on Freezing and Drying to discuss progress in this field since the first symposium held in 1951. The meeting is to be held in the Beveridge Hall, Senate House, London, W. C. 1., April 1-2. Some 20 speakers, including workers from France, Japan, Kenya, the U. S., and the U. S. S. R., have accepted invitations. The symposium will be open to all interested persons and information may be obtained from The Institute of Biology, 41 Queen's Gate, London, S. W. 7.

Course in Acupuncture in Vienna.—The "Österreichische Gesellschaft für Akupunktur," which represents the "Société International d'Acupunctur, Paris" in Austria, will present an elementary course of acupuncture May 16-22 in Vienna, Austria. The course will be held in English and will contain both theory and praxis. Admittance is limited to doctors and pregraduate students only. The course counts for the Austrian diploma of Acupuncture. To book course and lodging write Österreichische Gesellschaft für Akupunktur, Vienna XII, Tivolig. 73, before April 15. Interested persons will be asked to enroll on May 16, 10-12 a. m. The fee is $20 ($15 for students).

Audiology Congress in Italy.—The general secretaries of the International Society of Audiology have announced that the society's fourth congress will be held in Padua, Italy, Oct. 2-5. This meeting will be reserved for audiologists who are particularly interested in the progress of this specialty. Three round-table discussions are planned on the following subjects: "Auditory Prosthesis," "Traumas Caused by Noise," and "Cochlear Inde-

pendence." All correspondence regarding this congress should be addressed to the General Secretary, Fourth Congress of the International Society of Audiology, Prof. Arslan, Clinique O. R. L., Universitaire, Padua, Italy. It has been planned that the fifth society convention will be held in the spring of 1960 in Basel, Switzerland.

Biochemistry Congress in Vienna.—The fourth international Congress of Biochemistry, organized by the Österreichische Biochemische Gesellschaft under the auspices of the International Union of Biochemistry, will be held in Vienna, Austria, Sept. 1-6. The following symposiums are planned: Carbohydrate Chemistry of Substances of Biological Interest; Biochemistry of (1) Wood, (2) the Central Nervous System, (3) Steroids, (4) Antibiotics, (5) Morphogenesis, and (6) Viruses; Proteins; Physical Chemistry of High Polymers; Blood Clotting Factors; Vitamin Metabolism; and Insect Biochemistry. Two general lectures will be given at the opening and closing sessions by Prof. E. Chargaff, New York City, and Prof. A. E. Braunstein, Moscow, U. S. S. R., respectively. Colloquies on sulphur metabolism, biosynthesis of purines and pyrimidines, oxygenizing enzymes, and C_2-compounds in micro-organisms are scheduled. An exhibition of scientific apparatus, entertainment, excursions, and a ladies' program have been arranged. Registration fee is 320 Austrian Schillings (about $13) for active members. Those who intend to contribute a paper or a demonstration should register by May 1. For information write the General Secretariat, Wahringerstrasse 42, Vienna IX, Austria.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20, 1958. *Oral.* Philadelphia, April 23-26; San Francisco, June 18-21; Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part II.* Chicago, May 7-17. Final date for filing application was September 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written,* Jan. 26, 1959. Final date for filing application is July 1, 1958. *Clinical.* San Francisco, June 17-21; Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* April 3-4, Rochester, Minnesota, Denver, Colorado, Washington, D. C. Final date for filing application was Nov. 30. *Part II.* New York City, Jan. 29-31, 1958. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 6-9. Final date for filing application is March. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: San Francisco, June 30-July 2. Final date for filing application is May 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1042-1232 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Memphis, March 21-23; Atlantic City, May 3-5; Cincinnati, June 13-15; Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Peoria, Ill., June 20-21. Final date for filing application was Feb. 1. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Galveston, Texas, May 18-20. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Aviation Medicine,* Washington, D. C., March 20-22. Final date for filing application was December 30. *Occupational Medicine,* April 18-20. Final date for filing application was Jan 30. *Public Health* on a Regional Basis, April. Final date for filing application is Jan. 30. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: San Francisco, March 17-18; New York City, Dec. 15-16. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Special Examination in Nuclear Medicine for Diplomates in Radiology or Therapeutic Radiology,* Chicago, May 17. Deadline for filing application was Feb. 1. *Regular Examination in Radiology,* Chicago, May 19-23. Final date for filing application was Jan. 1. *Regular Examination in Radiology.* Washington, D. C., Dec. 8-12. Final date for filing application is July 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 225 So. 15th St., Philadelphia 2.

BOARD OF THORACIC SURGERY: *Oral.* Boston, May 12-13. Final date for filing application was December 1. The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

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GOVERNMENT SERVICES

AIR FORCE

Air Force Medical Conference.—The Air Force Medical Research Council held its third meeting in Washington, D. C., Jan. 21-22, 1958, with Major Gen. Dan C. Ogle, the surgeon general, opening the meeting. Among numerous subjects discussed were Special Experimental Space Indoctrination by Col. John P. Stapp, chief, Aero Medical Field Laboratory in New Mexico; Spatial Disorientation and Vertigo by Col. James P. Nuttall of the surgeon general's office; Ultraviolet Infrared and Cosmic Radiation by John L. Spencer of the Rome Development Center, New York; Blast Biology—Military and Public Aspects by Dr. Clayton S. White of the Lovelace Foundation, New Mexico. There was also a panel on aviation accidents and another on aviation and space medicine research. This council is designed to maintain a continuing survey of research requirements in aviation medicine and health sciences.

Surgeon General Ogle also attended the Air Force Command Surgeons Conference in Washington, D. C., Jan. 23, and with members of his staff discussed the structure, medical personnel, education, and physical standards of the future Air Force. Each of the many command surgeons present reported on the medical facilities under their personal jurisdiction.

VETERANS ADMINISTRATION

Personal.—Dr. George M. Leiby, manager, VA Research Hospital in Chicago, will be transferred as area director of professional services in the Columbus, Ohio, VA area medical office. Dan J. Macer, manager, VA Hospital at Sunmount, N. Y., will replace Dr. Leiby as manager of the hospital in Chicago, which is a 516-bed general medical and surgical facility. The hospital at Sunmount is a 515-bed facility for tuberculosis patients.

PUBLIC HEALTH SERVICE

Pneumonia Deaths Increase.—The surgeon general of the Public Health Service said on Feb. 7 that the number of deaths from influenza and pneumonia reported in 108 cities in the United States has been rising steadily for the past four weeks. Since the last week of December, they have steadily increased. The PHS Epidemiologic Surveillance Unit is working with state and local health officers to determine the cause. There was said to be no evidence of any widespread increase in Asian influenza cases throughout the United States. Small outbreaks, however, are continuing to occur in widely scattered areas, the most recent ones being reported from areas in New York, Texas, Iowa, Michigan, Illinois, and Georgia, as well as from several widely separated military installations in which the Asian influenza has been isolated. Asian influenza, the surgeon general said, may be smouldering in other areas throughout the United States. "This underscores the importance of second injections of Asian influenza vaccine for elderly persons and others in special risk groups. An examination of death certificates in several cities shows that a substantial number of influenza and pneumonia deaths are occurring among older persons."

National Conference on Air Pollution.—A national conference to study the problem of air pollution in urban areas is tentatively scheduled for the week of Nov. 15, 1958, in Washington, D. C., and is being called by recommendation of Dr. Leroy E. Burney, surgeon general of the Public Health Service. The purpose will be to bring together leading authorities to consider the many legal, medical, and industrial problems involved and to pool the experience already obtained by Los Angeles, Pittsburgh, St. Louis, and other cities in combating air pollution.

Legislation enacted in 1955 authorized the surgeon general of the Public Health Service to carry out a five-year program of research and technical assistance to the states on the growing air pollution problem. The surgeon general, who will preside over the conference, said that the conference would provide an opportunity for assessment of progress in midpoint of the five-year program.

Indian Health Chief Promoted.—Dr. James R. Shaw, chief, Public Health Service Division of Indian Health, has been promoted to the grade of assistant surgeon general, with a rank equivalent to that of rear admiral. Dr. Shaw is responsible for the administration of medical and public health services for about 380,000 American Indians and Alaskan natives. The Indian health staff of 4,500 includes physicians, dentists, nurses, sanitary engineers, medical social workers, and other administrative and technical personnel. Health services are provided in 56 hospitals and at more than 200 other locations. Dr. Shaw has been a member of the Commissioned Corps of the Public Health Service since 1938.

DEATHS

Bartholomew, James Kleckner, Chicago; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1887; on the staff of the Lutheran Deaconess Home and Hospital; died in Miami, Fla., Dec. 28, aged 95, of bronchopneumonia.

Bowers, Don DeLargy ● Indianapolis; Indiana University School of Medicine, Indianapolis, 1926; fellow of the American College of Surgeons; associated with the Indianapolis General and Methodist hospitals, and the St. Vincent's Hospital, where he died Dec. 5, aged 55, of a cerebrovascular accident and hypertension.

Boyle, Joseph Patrick, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1917; veteran of World War I; served on the staff of St. Vincent's Hospital for Women and Children; died in the Fitzgerald Mercy Hospital, Darby, Dec. 9, aged 71.

Bull, Stephen W., Spencer, W. Va.; Maryland Medical College, Baltimore, 1903; an associate member of the American Medical Association; veteran of World War I; on the staff of the Gordon Memorial Hospital, where he died Dec. 27, aged 89, of complications resulting from injuries sustained in a fall.

Bumgarner, James Irwin ● Millers Creek, N. C.; Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, 1950; member of the American Academy of General Practice; veteran of World War II; county health officer; medical examiner for Wilkes County and district pathologist; on the staff of the Wilkes General Hospital in North Wilkesboro; died Dec. 5, aged 39, of a cerebral hemorrhage due to a head injury from a fall.

Cadwallader, Seth Iredell, Mechanicsburg, Pa.; Jefferson Medical College of Philadelphia, 1900; an associate member of the American Medical Association; past-president of the Cumberland County Medical Society; died in Harrisburg (Pa.) Hospital Dec. 8, aged 83, of myocardial infarction.

Leddy, Eugene Thomas ● Rochester, Minn.; born in Taunton, Mass., Sept. 27, 1892; Harvard Medical School, Boston, 1919; since 1937 associate professor of radiology at the Mayo Foundation, Graduate School, University of Minnesota, where he became an instructor in radiology in 1929 and in 1933 advanced to assistant professor; from 1920 to 1922 an assistant at the Memorial Hospital in New York City, and from 1922 to 1925 head of the roentgen ray department of the Philadelphia General Hospital; for six months in 1925 carried on private practice of roentgenology in Providence, where he was head of the x-ray department of the Rhode Island Hospital; came to the Mayo Clinic on Oct. 1, 1925, as a first assistant in therapeutic roentgenology; on April 1, 1929, was appointed a consultant in therapeutic roentgenology and in 1948 was appointed head of the section on therapeutic radiology, a post held until 1953, when he became a senior consultant in therapeutic radiology; specialist certified by the American Board of Radiology; fellow of the American College of Radiology; member of the American Roentgen Ray Society, the Radiological Society of North America, American Radium Society, the Alumni Association of the Mayo Foundation, and the Society of the Sigma Xi; past-president of the Minnesota Radiological Society; an honorary member of the Old Blockley Medical Society of Philadelphia; on the staffs of the Methodist Hospital and St. Mary's Hospital, where he died Jan. 5, aged 65, of a cardiovascular accident.

MacLean, Hugh, La Jolla, Calif.; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1906; fellow of the American College of Surgeons; died Jan. 1, aged 79.

Macrae, James Gilbert ● Coldwater, Mich.; Washington University School of Medicine, St. Louis, 1910; member of the Iowa State Medical Society; for many years practiced in Creston, Iowa, where he was medical director of the Greater Community Hospital; veteran of World War I; died Jan. 1, aged 73, of cerebral vascular accident.

Merrifield, Frederick William ● Wilmette, Ill.; born in Plymouth, England, Aug. 4, 1887; Northwestern University Dental School, Chicago, 1916; Northwestern University Medical School, Chicago, 1931; associate professor emeritus of surgery at Northwestern University Medical School and professor of oral surgery emeritus at Northwestern University Dental School; served as chairman of the executive committee, Northwestern University Cleft Lip and Palate Institute; specialist certified by the American Board of Plastic Surgery; member of the American Association of Plastic Surgeons and the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; associated with the Evanston (Ill.) Hospital, Passavant Memorial, and Children's Memorial hospitals; died Jan. 6, aged 70, of uremia and chronic pyelonephritis.

● Indicates Member of the American Medical Association.

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Miller, Harry ✱ Schenectady, N. Y.; Long Island College Hospital, Brooklyn, 1919; past-president of the Schenectady County Medical Society, of which he was at one time treasurer; associated with St. Clare's Hospital, City Hospital, and the Ellis Hospital, where he died Jan. 2, aged 60, of cerebral hemorrhage.

Mitchell, Oliver L., Oak Park, Ill.; Northwestern University Medical School, Chicago, 1893; died in the Chicago Wesley Memorial Hospital Jan. 3, aged 88, of congestive heart failure and arteriosclerotic heart disease.

Nelson, Nesmith Perry ✱ Minneapolis; George Washington University School of Medicine, Washington, D. C., 1910; member of the Association of Military Surgeons of the United States; veteran of World War I; an organizer and board member of First Federal Savings and Loan Association; formerly practiced in Brainerd, where he was on the staff of St. Joseph's Hospital; died Dec. 14, aged 80, of cerebral vascular accident.

Newsam, Hugh Ernest, New York City; Meharry Medical College, Nashville, Tenn., 1933; associated with the health department of New York City; on the staff of the Harlem Hospital; died Dec. 17, aged 56, of cerebral hemorrhage.

Nicholson, James Willard ✱ Porterville, Calif.; Vanderbilt University School of Medicine, Nashville, Tenn., 1913; formerly associated with the Indian Service; served as city health officer; on the staff of the Porterville City Hospital; died Dec. 4, aged 70, of carcinoma of the prostate.

Noell, Robert Leonard ✱ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1928; specialist certified by the American Board of Orthopaedic Surgery; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; clinical professor of orthopedic and fracture surgery at his alma mater; veteran of World War II; on the staffs of the Wesley Hospital and St. Anthony Hospital, where he died Dec. 10, aged 58, of carcinoma of the liver.

Ornstein, Felix, Secaucus, N. J.; Medizinische Fakultät der Universität, Vienna, Austria, 1912; associated with Beth David Hospital in New York City and the Hudson County Hospital for Mental Diseases; died Dec. 18, aged 71, of coronary occlusion.

Oster, Edwin Arthur ✱ Los Gatos, Calif.; University of Illinois College of Medicine, Chicago, 1950; interned at San Joaquin General Hospital in French Camp; died Dec. 20, aged 34.

Otis, Eleanore Mabel Howe ✱ Moline, Ill.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; formerly served on the board of education; associated with Lutheran and Moline Public hospitals, and St. Anthony Hospital in Rock Island; died Dec. 27, aged 87, of cerebral thrombosis.

Parrott, John Samuel ✱ Pineville, Ky.; St. Louis College of Physicians and Surgeons, 1927; served on the board of education of Bell County; died in Oak Ridge, Tenn., Nov. 1, aged 61, of cancer.

Pasternacki, Arthur Sylvester ✱ Adrian, Mich.; Detroit College of Medicine and Surgery, 1929; formerly practiced in Wyandotte, where he was a city physician; veteran of World War II; on the staff of the Emma L. Bixby Hospital; died in Ann Arbor Dec. 22, aged 55, of carcinoma of the lung.

Ritze, John Adam, Midlothian, Ill.; Northwestern University Medical School, Chicago, 1911; died Jan. 1, aged 73, of coronary occlusion.

Rossiter, Perceval Sherer, Surgeon General, Rear Admiral, U. S. Navy, retired, Santa Barbara, Calif.; born in Shepardstown, W. Va., Nov. 30, 1874; University of Maryland School of Medicine, Baltimore, 1895; veteran of the Spanish–American War; on Jan. 20, 1903, appointed acting surgeon in the U. S. Navy; advanced through the commissioned ranks of the medical corps of the U. S. Navy, attaining the rank of captain on June 5, 1924; on March 17, 1933, was appointed surgeon general of the Navy with rank of rear admiral, serving until Dec. 1, 1938; transferred to the retired list, having reached the statutory retirement age of 64 years; during his active service of more than 35 years served with distinction throughout the United States and abroad and in ships of the fleet; a member of the U. S. Naval Mission to Brazil from 1922 to 1926; from 1939 to 1949 served as chief of staff at Gallinger Hospital, Washington, D. C.; fellow of the American College of Physicians and the American College of Surgeons; service member of the American Medical Association; past-president of the Association of Military Surgeons of the United States and Canada; director of the Tri-Counties Blood Bank; died Dec. 20, aged 83, of coronary occlusion.

Young, William James ✱ Auburn, Maine; born in Boston in 1881; University of Pennsylvania School of Medicine, Philadelphia, 1911; member of the American Public Health Association and the Association of Military Surgeons of the United States; veteran of World Wars I and II; served as health officer of the city of Waterville, college physician and coach at William and Mary College in Williamsburg, Va., athletic director at the University of Maine, and for a year medical examiner at A. and M. College at College Station, Texas; until his retirement, district health officer of Androscoggin, Franklin, and Somerset counties; died suddenly in Central Maine General Hospital in Lewiston, Dec. 8, aged 76, of aneurysm of the abdominal aorta.

FOREIGN LETTERS

BELGIUM

Health Survey in Belgian Congo.—De Smet *(Bruxelles-Medical)* studied stool specimens of the population in the Belgian Congo and found evidence of ancylostomiasis in 60.6% of the Belgians. In the nontreated natives such evidence was found in 77.2%, and in the Topoke tribe in 90%. The malarial parasite index in the Belgian population has been reduced from 70% to 15%. In dealing with the Bantu tribe, the direct approach was helped by the psychological bent of the people who believe that the seat of the disease should be attacked directly, preferably by means of a needle. Thus it was possible to obtain many needle biopsies of the liver among these people. The author considered this method as an indispensable part of clinical investigation of hepatic damage. The puncture biopsy may be negative if the needle passes through healthy tissue adjacent to a cirrhotic nodule or tumor but the likelihood of this can be reduced by repeating the puncture.

This method has, however, the disadvantage of occasionally showing an aspect that is difficult to interpret because the relations with the clinical symptoms (e. g., inflammatory infiltration of the portal space) are not sufficiently known. It is especially valuable if repeated after recovery, thus enabling one to exclude the persistence of a latent hepatic syndrome such as is seen in patients with postnecrotic cirrhosis. It may also indicate the regression of histological changes after medical or surgical treatment. In the author's series of 540 needle biopsies of the liver (128 patients had repeated biopsies), about 140 specimens were classified as normal. The liver flocculation test had no specific value for estimating liver function. Studies by means of hepatography are still in the experimental stage and do not seem to offer a sensitive test in syndromes not associated with severe parenchymatous damage. The author believed that a good clinical examination and histological studies provided the best index for evaluating the condition of the liver in the Negro.

Vascular Purpura.—At the Journées Médicales in 1957, Jean Bernard stated that he had produced a syndrome in animals which was closely related to acute vascular purpura which may be allergic or idiopathic. Chronic inflammatory or recurrent purpura must be distinguished from these two forms. The speaker gave an intramuscular injection of rabbit serum sensitized to guinea pig endothelial cells to guinea pigs, and an acute vascular purpura resulted. If the sensitized rabbit serum is injected intradermally, the only result is a local ecchymosis. Human serum from patients with idiopathic purpura produces the same toxic effect on guinea pig capillaries. It is believed that the vascular endothelium is capable of reacting to certain insults in the same way as the leukocytes and the platelets, i. e., that they are injured by the contact with antibodies of endogenous or exogenous origin, and under certain conditions auto-antibodies may develop.

Logopedics.—M. Mussafia of the Mental Hygiene Department of the Belgian Red Cross reported in *Le Scalpel* that most of the patients seen by the logopedic service were stammerers. The therapeutic approach is based on the fact that speech is a manifestation of personality. Reeducation must be directed toward the entire person, not just his stammering. The stammerer must rediscover the possibility of a normal contact with other people, even though this has been lost since earliest childhood.

BRAZIL

Pathogenesis of Oliguria due to Carbon Tetrachloride Poisoning.—Dr. Armando V. Rotondi, at a meeting of the Associação Paulista de Medicina, reported that he had injected carbon tetrachloride into the portal vein of rats. This caused a marked oliguria or even anuria in the acute phase of the massive hepatic necrosis. He found no correlation between the histological changes in the kidneys and the degree of oliguria. The determination of the arterial tension in animals with acute hepatosis, 24 hours after the portal injection of carbon tetrachloride, showed variable degrees of diminution of the tension. Animals with arterial tensional values insufficient to create effective positive pressure to determine glomerular filtration presented a greater diuresis than that shown by animals with smaller reduction of the arterial tension. In other cases, animals with normal arterial tension had intense oliguria. The eventual circulatory shift (Trueta's shunt), shown by a cortical ischemia with medullar vasodilatation, was also investigated in experimentally poisoned animals in the phase of oliguria. After an injection of carbon black ink into the aorta,

The items in these letters are contributed by regular correspondents in the various foreign countries.

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all cortical and subcortical glomeruli appeared colored by the ink, thus evidencing the nonexistence of a circulatory shift and the ischemia of the cortex.

Finally, the author injected normal rats intraperitoneally with 2 ml. of normal rat serum. This was followed by a retention of 1.15 ml. of water per 100 Gm. of body weight. A similar injection of 2 ml. of serum from rats with massive necrosis of the liver caused a water retention of 3.17 ml. per 100 Gm. He concluded that these results demonstrated the existence of an increase in antidiuretic hormone in the serum of rats with massive necrosis of the liver, this humoral change explaining the pathogenesis of this hepatorenal syndrome whose renal morphologic characteristics are typical of lower nephron nephrosis.

Fetal Anoxia.—Dr. Luis A. Correa da Costa (*Anais brasileiros de ginecologia*, vol. 44, 1957) reported a series of 200 consecutive autopsies on fetuses whose cause of death was anoxia. In this series 72 were judged to be dead before the mother was admitted to the hospital, and 6 were dropped from the study (3 with anencephalus, 1 with hydrocephalus and spina bifida, 1 with hydrops fetalis, and 1 because of xiphopagus). Of the remaining 122 fetuses, 8 died in the antepartum, 74 in the intrapartum, and 40 in the postpartum period. Of these 122 fetuses, 88 were premature. In the total group of 200, the most frequent causes of death were convulsive and nonconvulsive toxemia in the mother in 75, complications of the umbilical cord in 50, forceps application in 29, breech presentation in 22, and delayed labor in 17. Toxemia may have been present in a larger number since, in the cases of fetuses who were dead before admission, the clinical signs of toxemia in the mothers might already have disappeared.

Vaginal Hysterectomy.—Dr. Rosalvo C. Cavalcanti (*Revista de gynecologia e d'obstetricia*, vol. 100, 1957) analyzed 40 cases of vaginal hysterectomy for uterine prolapse. In 32 there was third degree; in 6, second degree; and in 2, first degree prolapse. The age of the patients varied between 29 and 74 years (average 49.5). Sixteen patients had had more than five pregnancies. The only death in the series occurred suddenly 10 days after the operation and was caused by cerebral hemorrhage.

INDIA

Indian Public Health Association.—At the second annual meeting of the Indian Public Health Association in December in Calcutta, the director-general of health services of India suggested the establishment of full-time departments of social and preventive medicine in all medical colleges because preventive and social medicine should be taught not as something apart from clinical instruction but as an integral part of medicine as a whole. He urged that the public be educated to appreciate the importance of disease prevention. He requested the authorities to adopt a more realistic attitude in the matter of emoluments for the staff in rural areas where personnel were not easy to find owing to poor wages and lack of amenities.

Multiple Worm Infection.—Patel and Kamat (*Current Medical Practice*, vol. 1, December, 1957) treated 18 patients who had multiple helminthic infections with tablets each containing 186 mg. of hexylresorcinol and 500 mg. of piperazine citrate. Six of these patients were asymptomatic, seven had abdominal pain and/or diarrhea, one had anemia and signs of nutritional deficiency, and four had abdominal symptoms, generalized pains, and weakness. Both a routine and formalin-saline concentration method were used for the stool examinations. Five of the tablets were given on an empty stomach followed by a saline purgative next morning. Stools were examined on the 4th, 8th, and 15th days. If they remained positive on the 21st day, the treatment was repeated. This procedure was used 17 times on 13 of the patients, only 2 of whom were cured. The treatment was a total failure in seven and unsatisfactory in the remaining nine. Hexylresorcinol by itself is effective against ascariasis and slightly less so against ancylostomiasis. Piperazine is even better against round worms but, surprisingly, a combination of the two failed to cure these infections.

Tuberculous Meningitis.—K. I. Vyas (*Indian Journal of Child Health*, vol. 6, December, 1957) analyzed 120 cases of tuberculous meningitis. The highest incidence was seen between the ages of six months and four years and 90 of the patients were boys. The disease was most common among poor and lower middle class families, about 90% belonging to these groups. There was no seasonal variation. About 33 patients came from villages and the rest from cities. The nutritional status of the affected children was poor in 70%, fair in 20%, and good in 10%. History of contact with a tuberculous patient was available in only eight cases. Measles was the commonest precipitating factor, a history of this disease being present in 31 patients. A history of whooping cough was present in 14, recent trauma to the head in 6, and chronic diarrhea in 5. Nineteen patients were admitted in the early, 39 in the intermediate, and 62 in the late stage of the disease. The diagnosis was made from typical spinal fluid findings and associated evidence of active tuberculosis elsewhere in the body. Fifty patients had associated intrathoracic tuberculosis; 34, intra-abdominal lesions; 32, intratho-

racic and intra-abdominal lesions; and 4, tuberculous cervical glands. The onset was acute in 65 patients and gradual in the rest.

The commonest mode of onset was with fever and convulsions; other symptoms noticed at the onset were vomiting, lethargy, coma, headache, paresis, restlessness, constant crying, sleeplessness, irritability, anorexia, apathy, delirium, drowsiness, and retention of urine. The earliest symptoms were changes in mood and behavior in a previously active and happy child. A lumbar puncture at this stage should give evidence of the disease when there is still a chance of recovery without residual damage. Fever was continuous from the preceding attack of measles or whooping cough in 12 patients. Terminal hyperpyrexia was seen in 31 patients; convulsions in 90; vomiting in 68; cough in 66; and headache in 20 (mostly in the higher age group). Other symptoms were tremors, constant movements of extremities, pain in the neck, excessive perspiration, and trismus. Lethargy was present in 30 and coma in 58. Grinding of the teeth was noticed in nine and retention of urine in five patients; these five were comatose. A vacant stare was observed in 16, and a meningeal cry was heard in 7 of the comatose patients. A palmar and/or plantar rash was seen in 20. Tache cérébrale was observed in 50% of the patients, and most had tachycardia. On admission 20 had dyspnea and in 26 the breathing was irregular. There was marked spasticity with opisthotonos in 14, moderate spasticity in 48, and flaccidity in 13. Nuchal rigidity was present in 61, Kernig's sign could be elicited in 30, marked head retraction was present in 13, bulging fontanels in 12, and hydrocephalus developed in the course of the disease in 7. Deep reflexes were exaggerated or absent in the deeply comatose patients. Myotatic irritability was elicited in 11. Changes in the eyes included internal deviation of the eyeballs, nystagmus, choroid tubercles, sluggish or absent reaction of pupils to light, dilated pupils, and hippus.

Patients with prolonged coma developed decerebrate rigidity and these usually died. Paresis was seen in 10 and aphasia in 7. Facial paralysis was seen in 23 patients. In 13 the optic nerve was affected, resulting in diminished vision or blindness. Otitis media was present in five. Signs of vitamin deficiency were seen in 68. The liver was palpable in 48 and the spleen in 8. Eleven had nutritional edema. Half of the patients died. The mortality was highest in those under the age of three years. The younger the patient, the worse the prognosis. Treatment started in the late stage of the disease had a poor chance for success and even if patients treated late survived, they invariably had some neurological residual damage such as paresis, mental deficiency, hydrocephalus, facial paralysis, squint, diminished vision, and increased psychomotor activity.

The Influence of Hormones on Testicular Changes.—C. M. Rangam and co-workers (*Indian Journal of Medical Sciences*, vol. 11, December, 1957) reported the results of their experiments on rats to determine whether testosterone will prevent or retard postvasectomy tubular degenerative changes in the testes and whether estrogen will enhance or augment these changes. A series of 34 male albino rats including 18 controls were used. Vasectomy was performed on the 16 experimental animals. The hormones were given to batches of rats in both groups and the changes studied for six weeks. The control animals receiving testosterone and estrogen showed no testicular change. The experimental animals not receiving hormones showed degeneration of the tubular epithelium in the first and second week, regeneration at the end of fourth week, and complete restoration to normal after six weeks, as was expected. Administration of testosterone prevented this tubular degeneration after vasectomy but it did not promote spermatogenesis. Estrogen delayed the onset of tubular degeneration and reduced the intensity of degeneration that occurred eventually. It also led to retardation of repair in the degenerated tubules. Thus, prolonged administration of estrogen may antagonize the action of testosterone in the process of repair. The histochemical changes ran parallel with the histological alterations.

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JAPAN

Fasting as a Therapy.—Fasting is being widely prescribed as a panacea by various lay and religious groups. The first day patients are given a bowl of rice gruel; on the second, a bowl of rice water morning and evening; and from the third day on, nothing but water. Patients with mild illnesses are so treated for a week then sent home as cured. More serious illnesses are thus treated for a month or longer. No drugs are given. The following case is illustrative. A man with chronic dyspepsia was admitted to such a "hospital" and on the second day vomited some brown materials. His condition steadily deteriorated and his wife had him transferred to a regular hospital where he died two days later. After a review of the circumstances, it will be decided whether the man operating the first "hospital" was practicing medicine without a license and whether he should face a charge of manslaughter.

Cancer and Rice.—Dr. Will Mayo is credited with the belief that the disparity in the incidence of death due to gastric cancer between men and women in Japan was largely due to the fact that the husband hurriedly ate a steaming bowl of hot rice and rushed off to work while the wife enjoyed a leisurely breakfast afterward. In Dr.

Mayo's day the statistics supported this theory. Gastric cancer affected several times as many men as women but today, strange as it may seem, the death rate in both sexes is about the same. Furthermore fully 50% of all the deaths from cancer are due to gastric cancer despite the fact women have a relatively high death rate from uterine and mammary cancers. With the publication of these figures, a new theory had to be proposed. Theorists now say that there lurks in the very essence of rice the cause of stomach cancer. They would now curtail rice consumption in general and replace it in part with wheat. They point to the fact that Hawaiians of Japanese ancestry have a low mortality from gastric cancer, possibly because they prefer bread to rice.

Faith Cures.—Medical practice here is invaded on many fronts by irregulars, eclectics, and various cultists. A typical case is that of a school boy who sustained a head injury in a wrestling match. The ill-advised parents took him to a faith healer; 36 hours later the boy was in a coma and in another 24 hours he was dead. A simple operation to remove a subdural hematoma might have saved him. Because the sick and injured are often taken first to a faith healer, the physician may see them too late to be able to save them. The blame for failure is then often unjustly placed at the door of physicians. With a view to correcting this situation, the government has launched a campaign for a universal health and accident insurance covering the remaining 15 million people not yet insured.

NEW ZEALAND

Thoracic Trauma.—Dr. J. Borrie (*Australian & New Zealand J. Surg.* **26**:229, 1957) laid down the following principles for the management of major thoracic trauma: (1) give oxygen and secure the airway, (2) relieve intrapleural tension, (3) relieve the pain, (4) stabilize the chest wall, (5) give blood as required, and (6) explore the chest when indicated. Although theoretically if these rules are applied all patients should recover, in practice this is far from being true. In a series of 30 patients with chest injuries, 10 had suffered a violent accident. Six of these died; three within 6 hours, two within 19 hours, and one after three days. The author investigated the reasons for these deaths. The accidents that caused these fatal injuries included being crushed between an automobile and a bus, being thrown from a motorcycle, being hit by a truck, crashing down an embankment in a truck, being struck by a railway engine, and being tossed by a bull.

The following plan for management was suggested: as first aid, if there is a compound fracture, especially with pneumothorax, cover the wound with a large "shell dressing," and firmly strap it to the chest wall with several strips of elastoplast; remember the possibility of associated lesions, especially spinal injuries; always move the patient carefully; and avoid giving morphine as this further embarrasses respiration. On admission to the hospital, if respirations are seriously embarrassed, emergency tracheotomy and intercostal drainage may be required. Only after this should roentgenograms of the chest be made and further treatment given. Having seen the rapid improvement that occurs when thoracotomy is performed for those with compound fractures, as well as having had the opportunity of suturing the torn lung and evacuating a hemothorax, the author recommends clinical and radiologic localization of the lesion and thoracotomy for all serious chest injuries. Sterile tracheotomy, intercostal drainage, chest aspirating, and bronchoscopy sets should be available in all emergency rooms.

Tendon Transplants.—At a Meeting of the Otago Medical School Research Society (abstracted, *Proc. Univ. Otago Med. Sch.* **35**:25, 1957) Dr. N. W. Nisbet reported that, in spite of some claims by European authors, homogenous transplants do not survive in the rabbit, guinea pig, and rat and that it may be inferred that this also applies to most adult mammals, including man. Transplants were obtained from the tendo achillis of a suitable donor under aseptic conditions and transplanted immediately into a gap in the tendo achillis of the recipient. Atraumatic needles and stainless steel wire were used for the tendon suture, and in the rabbits a plaster cast was applied and retained for three weeks. The animals were killed at intervals of one week to several months. Macroscopically a fibrinous structure formed, which enveloped the transplant and became adherent to it. Later it became apparent that the transplant was inert and was pushed aside by the regenerated tendon. Ultimately it became a small opaque body on the surface of the latter.

The microscopic findings were mainly those of regenerating tendon from the host's tissues. The cells of the transplant degenerated and died, the center became necrotic and fragmented, and the normal fibrillar structure of the tendon was lost. The transplant was embedded in the longitudinally disposed cells and vessels of the regenerating tendon but added nothing to the reparative process. The unstained injected preparations showed clearly that no capillaries penetrated the transplant. The stained sections showed that vessels penetrated the transplant only as part of the granulation tissue involved in its absorption. The surrounding host tissues responded to the implants by an immune reaction, the severity of which varied between the animals, being greatest in the guinea pig and least in the rat. Dr. Nisbet concluded that homogenous

tendon is capable of producing an immune response that varies in time of appearance, duration, and intensity in various animals. The transplants do not survive, and a successful functional result is due to tendon regeneration.

Drug Cost in the Health Service.—In a note circulated to all physicians the health department pointed out that the heaviest drain on available funds came from the costly preparations frequently prescribed. An analysis of 21,000 prescriptions from the Wellington area was made. The most expensive items included tetracycline, acetazolamide, phenylbutazone, sulfisoxazole (tablets and syrup), penicillin V (tablets and suspension), alseroxylon, reserpine, chlorpromazine, chloramphenicol (capsules and palmitate), propantheline, ethisterone, diphenylhydantoin (tablets and capsules), vitamin B_{12} with intrinsic factor concentrate, chlorcyclizine, amesec, and sulfamethizole. The most expensive prescriptions were those for tetracycline and chloramphenicol capsules. These two preparations alone cost the health service about $1,050,000 a year. Physicians are asked to consider whether plain penicillin, which is safer and cheaper, and a sulfonamide would not be better treatment than a broad-spectrum antibiotic in some cases.

Stillbirths and Neonatal Deaths.—The obstetric research committee is investigating the causes of stillbirth and neonatal deaths. Under international agreement all members of the profession practicing obstetrics are asked to complete a form in all cases of stillbirth from the 20th week of gestation on. The committee recommends that whenever a diagnosis is in doubt an autopsy of the stillborn child be conducted. This can be done in all the large centers by a pathologist and is free of charge to the patient and doctor. In smaller centers or country districts, the physician concerned can perform the autopsy. This procedure should not only help the physicians but should also be of great comfort to the parents. In many cases of stillbirth if no external abnormality is evident, there is always a possibility that internally some severe anatomical defect can be found to explain the death. Unless a fetus is markedly macerated an autopsy should be performed and the committee suggests that an examination of the placenta be made at the same time.

UNITED KINGDOM

Deaths Due to Antibiotic-Resistant Organisms.—The Public Health Laboratory Service of London is investigating a number of deaths that occurred during the influenza epidemic from infection by organisms resistant to penicillin and other antibiotics. In these cases death occurred rapidly within a day or two. In some hospitals wards have been closed and disinfected and only the most urgent cases admitted. Two babies died from infection in the Royal Maternity Hospital, which was then closed temporarily. Staphylococcic infection was diagnosed in a number of persons who died in the recent influenza epidemic. Fifteen died in an old people's home, probably as a result of such infection. The influenza virus paves the way for the streptococci also, infection from which may rapidly prove fatal.

Pheochromocytoma of the Bladder.—Lumb and Gresham (*Lancet* 1:81, 1958) stated that pheochromocytoma of the bladder is a rare condition. Theirs is the third case reported. The tumor may produce pressor amines giving rise to striking clinical findings. The patient was a woman of 48 who at the age of 13 began to have curious attacks of extreme palpitation, bursting headaches, pallor of the face and hands, sweating, and coldness of the extremities after micturition. These attacks lasted only a few minutes and ceased with the menarche. They reappeared when the patient was 41 and gradually increased in frequency and intensity, until they occurred after every act of micturition and lasted half an hour. On the admission of the patient, her blood pressure ranged from 160/100 to 230/110 mm. Hg. As the basal metabolic rate was +33% and there was an equivocal response to phentolamine, a diagnosis of paroxysmal tachycardia occurring in a patient with hyperthyroidism and hypertension was made. Several years later a prolonged bout of hematuria led to readmission and cystoscopy. A smooth tumor was observed in the bladder, and as the urine was found to contain 0.8 mg. of levarterenol bitartrate per milliliter, the authors thought that it might be a pheochromocytoma. The tumor was removed, the blood pressure being controlled with phentolamine and levarterenol. It had the appearance of a pheochromocytoma and contained 2.3 mg. of epinephrine and levarterenol per gram. The symptoms disappeared after the operation. The attacks were attributed to the squeezing of the tumor and liberation of pressor amines by contraction of the bladder muscles.

Penicillamine and Hepatolenticular Degeneration.—It is now established that in patients with hepatolenticular degeneration there is an inability to synthesize the copper-binding serum-protein ceruloplasmin, with the result that the plasma copper is low and there is increased excretion of copper in the urine. Walshe showed that penicillamine hydrochloride given by mouth in doses of 1.5 Gm. daily promotes the excretion of copper in patients with this disease, and with Osborn (*Brit. M. J.* 1:70, 1958) he investigated by a tracer technique the comparative merits of penicillamine and dimercaprol in promoting cupruresis in this condition. The excretion of an injected dose of 100 μc of Cu^{64}

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was followed in a normal subject and in three patients with lenticular degeneration before and after oral treatment with penicillamine and intramuscular injections of dimercaprol. Determinations of urinary copper were made by chemical and radioactive methods. It was found that penicillamine actively increased the excretion of copper, being superior to dimercaprol in this respect. Most of the injected copper was concentrated in the liver within 10 hours in the normal subject, reaching a mixmum of more than 90% and decreasing steadily to 70% by 50 hours. In the patients with lenticular degeneration, however, the concentration of copper in the liver never exceeded 50%. These results support the currently held theory of copper metabolism, that in normal persons almost all the ingested copper in the body is firmly bound to protein within 24 hours, whereas in lenticular degeneration it mixes with a large body pool of copper and not being bound is largely excreted into the urine by the glomeruli.

Intraglossal Injection.—In the treatment of unconscious or anesthetized patients it is often necessary to give intravenous injections. In the obese or collapsed patient it may be impossible to find a vein, and intramuscular injections may require 10 minutes or more to take effect. The alternative is to give the injection into any highly vascular organ to obtain a rapid effect. Such an organ is the tongue. Bullough (*Lancet* 1:80, 1958) used the tongue in unconscious patients in emergencies and in anesthetic practice when veins were inaccessible or collapsed. The onset of action after intraglossal injection is 45 to 90 seconds, or almost as quick as that after an intravenous injection. The needle is inserted by way of the ventral surface because bleeding on its withdrawal is less common at this site. Care is taken to avoid the sublingual veins on either side of the midline. Provided a sharp 16 to 18-gage needle is used there is little bleeding on withdrawal of the needle. Volumes up to 2 ml. can be given in this way. Bullough warns against the injection of irritant solutions, such as soluble barbiturates, phenothiazine derivatives, or strong solutions, except as a life-saving measure.

Congenital Galactosemia.—Hitherto the inability of some infants to metabolize galactose normally has not been discovered until the signs and symptoms of galactosemia have been produced by the ingestion of milk. The clinical syndrome, which includes mental deficiency, could be avoided if the condition were diagnosed at birth before milk is given. A galactose-tolerance test may be dangerous for a child with congenital galactosemia. Schwarz and co-workers (*Lancet* 1:24, 1958) devised a method of detecting congenital galactosemia just after birth by using cord blood. Their method is based on the observation that incubation of galactosemic erythrocytes with galactose leads to accumulation of galactose-1-phosphate in the cells. The amount of the latter that accumulates in normal erythrocytes in such circumstances is much smaller. The erythrocytes are incubated first with galactose and then with glucose. The free sugar is then washed out with saline solution, and after removal of protein the total organic and inorganic phosphates are precipitated as barium salts, and the galactose and glucose-1-phosphates selectively hydrolyzed to free galactose and glucose. These sugars are separated chromatographically, and the amount of galactose is estimated by comparison with known quantities of the latter chromatographed simultaneously. The test can be made in the absence of any clinical signs or symptoms of congenital galactosemia and without a galactose-tolerance test. It would not be possible to carry out the test on all newborn infants, but it could be used in patients with a family history suggestive of the disease, or for confirming the diagnosis in untreated or suspected cases. The infant can then be given a galactose-free diet if necessary, and saved from the damaging effect of dietary galactose. Galactose can enter the fetal tissues in utero, even though it cannot be detected in the mother's blood.

Numismophagia.—Surgeons at Sedgefield General Hospital, Durham, recovered 424 coins and 27 pieces of wire from the stomach of a man aged 54. He survived the operation, during which 366 halfpennies, 26 sixpences, 17 threepenny pieces, 11 pennies, 4 shillings, and the wire, weighing a total of 5 lb. 1 oz., were removed. These were swallowed over a period of several years. The patient was admitted to hospital with a history of loss of weight and anorexia.

Adrenocortical Hormones and Surgery.—There is still a widespread belief that the administration of adrenocortical hormones adversely affects healing and resistance to infection, and that for this reason care should be exercised in giving them just before or after operations. Popert and Davis, (*Lancet* 1:21, 1958) however, showed that these hormones add no risk to operations, do not delay healing, and do not increase complications. They recorded the results of 36 operations performed on patients under treatment with adrenocortical hormones for rheumatoid arthritis and other collagen diseases. Immediately before the operation, all the patients were receiving cortisone, an analogue, or corticotropin in amounts sufficient to suppress at least partly the symptoms of their disease. The patients underwent orthopedic, abdominal, and ear, nose, and throat operations, cesarean section, mastectomy, repair of hernia, and multiple dental extractions. The dosage of cortisone varied from 75 to 100 mg. daily, and analogues were given in corresponding doses. Wound healing was normal, except

in two patients who were receiving corticotropin and who showed evidence of excessive adrenal stimulation at the time of operation. Bone repair was normal in the orthopedic cases. There was no evidence of exacerbation of peptic ulcers in those patients with this condition. Only two patients had slight superficial wound infections. In five patients on whom operation was performed in a septic field, no special precautions were needed, and resolution was rapid and uneventful. The authors concluded that operations performed during long-term treatment with adrenocortical hormones carry no increased risk of complications, provided there are no gross signs of overdosage, and the administration of the hormones is not interrupted.

Psittacosis.—Dr. Andrew Semple, health officer of Liverpool, claimed that the apparently harmless pastime of feeding pigeons in city squares may cause psittacosis. He and his staff found the virus in more than a third of the pigeons examined after a roundup of wild and tame birds. They believe that pigeons are a dangerous reservoir of disease. Many people feed pigeons. If they must do this, they should keep well away from the birds and not handle them. Two cases of psittacosis in one family were traced to homing pigeons. Those affected fed and fondled the birds. The virus is found in the nostrils and during preening reaches the feathers, from which it is transmitted to those handling the pigeons. Psittacosis is more common than is suspected, and is responsible for a number of cases of fever of unknown origin.

Neomycin for Hepatic Coma.—According to Sherlock and co-workers (*Lancet* 2:1263, 1957) the syndrome of hepatic precoma and coma in patients with liver disease is related to the absorption of toxic substances from the intestines that are probably derived from bacterial action on nitrogenous material. In order to diminish the intestinal action of bacteria in these patients the authors treated them with neomycin. Eight patients with cirrhosis and chronic portal-systemic encephalopathy and 12 patients with acute hepatic coma were given 4 to 10 Gm. of neomycin daily for as long as ten months. Six patients showed pronounced clinical benefit. Within a week the "flapping" tremor disappeared, coordination improved, and there was increased ability to perform mental function tests. Improvement was associated with a fall in the fasting arterial blood ammonium level and an improvement in the electroencephalogram. Fetor hepaticus disappeared in six of seven patients with chronic hepatic disease. Symptoms returned in some of the patients on stopping treatment with neomycin. With treatment, the stools became bulgy, pale, and usually odorless. Escherichia coli was not found in the stools of patients receiving neomycin for several weeks. The fecal flora returned to the pretreatment figure within a week of stopping of treatment. Diarrhea and oral moniliasis occurred as complications in some of the patients.

Neomycin is useful not only in controlling symptoms when restriction of dietary protein has failed but also in allowing a larger intake of protein. The success of the neomycin treatment confirms the suggestion that some product of bacterial action on protein in the intestine is at least partly responsible for the neuropsychiatric changes in some patients with liver disease. Unfortunately treatment is expensive, one month's supply of neomycin for one patient costing $220 at hospital rates.

Danger in Multiple Sclerosis Vaccine.—Dick and co-workers (*Brit. M. J.* 1:7, 1958) investigated a vaccine that Russian workers claimed to be effective in the treatment of multiple sclerosis. This vaccine consists of a formalinized suspension of the brains of rats or mice infected with the S. V. strain of a virus of acute encephalomyelitis of man. A specification has been drawn up by the State Medical Testing Laboratory, Moscow, and the vaccine is manufactured and distributed by the Metchnikoff Institute in Kharkov. The virus was recovered in the course of research on the cause of multiple sclerosis. The virus appears to be a rabies virus. The authors demonstrated Negri bodies in mice inoculated intracerebrally. They were unable to confirm the Russian claim of specific neutralization of the virus by serums from patients with multiple sclerosis. They pointed out that the Russian claim of a 30% improvement in patients with the disease treated with the vaccine was of the same order as the 44% of spontaneous remissions occurring in untreated patients. Owing to the possible danger of using a rabies vaccine, and its doubtful effectiveness in the treatment of multiple sclerosis, the authors warned against its use.

Anomalous Sedimentation Rates.—Shannon and Bywaters (*Brit. M. J.* 2:1405, 1957) stated that when the sedimentation rate was estimated by the Wintrobe method the incidence of misleading results was high enough to outweigh its advantages, which were mainly of a technical nature. They based their evidence on 19,000 sedimentation rates obtained by the Wintrobe method. Duplicate readings were made on 2,500 of these, using the Westergren method, the results being correlated with the clinical condition of the patient. Anomalous values from the Wintrobe method occurred in 4.6% of all readings. The erroneous results were shown to be due to the additive effects of the inadequate bore of the Wintrobe tube, a high plasma viscosity, and a hematocrit level above 40 ml. per 100 ml. As the hematocrit level increases above this figure, the incidence of erroneous results increases rapidly. No adequate method of correction based on the hematocrit level alone can be applied.

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CORRESPONDENCE

THE LAGGING OUTPATIENT DEPARTMENT —A PROBLEM IN HOSPITAL ORGANIZATION

To the Editor:—Improved physical facilities and more scientific methods for diagnosis and treatment have been resulting in progressively better care for the inpatient, while the outpatient, it is generally admitted by modern students of the subject, has been denied many of the benefits of organizational progress in the general hospital. One cannot stress too strongly the need for creating conditions under which outpatient clinics—those stepchildren of the hospital family—can be enabled to give a higher quality of care. Clearly, the emphasis in the prevention and management of illness must also be felt by the ambulatory patient. The needs of the outpatient must be given at least equal consideration with those of the inpatient. Where the outpatient clinic is lacking in the essentials for diagnosis and treatment by a competent medical staff, preventive opportunities may be lost until illness reaches an advanced stage. A higher quality of service in the early stages of illness may lessen the need for hospitalization, and the continuing of the care of patients on their discharge from the wards may help to clinch the cure.

The high and progressively increasing cost of inpatient care should, in itself, compel the improvement of the care of patients in outpatient clinics. In a typical large voluntary hospital in New York City the cost of hospital care per patient-day is approximately $26; outpatient care comes to $6 per visit. Any plan for improvement, however, must be based on a thorough analysis of existing conditions of service. For this purpose an up-to-the-minute study of selected clinics by a mixed group of skilled professionals is proposed. Since the internal-medical clinic is usually the distributing center for the outpatient service as well as a screening clinic for admission to the wards, such a study might well begin with this department. It should aim toward equalizing inpatient and outpatient care and should include an estimate of costs in relation to the financial possibilities of the hospital.

Subjects to be studied with particular care should be records and organization and their relation to inpatient service, including information on patients referred to and from hospital and clinic, with reasons for the transfer; laboratory service; equipment; conditions under which doctors serve patients; doctor-time per patient; auxiliary personnel available to the staff, such as secretaries, nurses, social service workers, dietitians, and interpreters; use of volunteer help; and adequacy and arrangement of space for waiting rooms and examining rooms, with emphasis on privacy. Medical executives and hospital trustees could serve their communities better by undertaking such studies. If a representative communal organization covering a wider area than that of a single hospital will cooperate, a correspondingly greater influence on hospital policy can be expected. The medical profession owes it to itself to promote such an investigation.

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WHEEL CHAIRS

To the Editor:—The editorial on the wheel chair appearing in the Jan. 25, 1958, issue of THE JOURNAL, page 373, is a timely reminder that techniques and technical devices work better if the individual needs of individual patients are taken into account. As is stated, the patient requiring a wheel chair "will get the best wheel chair for his needs only if his physician takes the time to evaluate those needs."

Although the emphasis of the editorial was on the physical needs of the patient, his emotional needs are also of great importance and indeed may be crucial in determining the success or failure of his adaptation. In our striving, competitive culture, the wheel chair is a powerful symbol of dependency, often viewed by the disabled person with partly unconscious ambivalent feelings, the conscious component of which may be a rejection of the whole idea. A patient with this kind of conflict will feel resentment and despair, and it is very likely that he will have many bitter complaints about his wheel chair which no amount of adjustment of the chair itself will satisfy or that he will develop any of a variety of psychopathological states.

To the extent that the physician is aware of these psychological factors and their possible effects on his patient's ability to live with a wheel chair, he will be in a better position to meet his patient's real needs, emotional as well as physical. He will, in every case, attempt to understand something of the significance of the wheel chair to his patient, and, if negative or unrealistic attitudes are evident, he can do a great deal in helping the patient distinguish symbolic bugaboos from his own real best interests. In some cases it may even be advisable to defer the prescription of a physically needed wheel chair until the patient has become better able to accept it for what it is and what it can do for him.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Weight to Be Given to Paternity Test in Bastardy Case.—The complainant, an unmarried woman, filed a bastardy proceeding in which she alleged that the defendant was the father of a child previously born to her. The defendant pleaded not guilty and filed a motion for a blood test of the child, which was granted. The case was heard in the juvenile court of Ohio.

At the trial, the defendant objected to being called on cross-examination on constitutional grounds and his objection was sustained. Furthermore, he did not testify on his own behalf. The only witness he called was the doctor who had been appointed by the court to make the blood grouping tests. Dr. Marsters, a clinical pathologist, specialized in blood groups. He was head of clinical chemistry at Cleveland City Hospital and in charge of its blood bank. He was also assistant professor of biochemistry in the Department of Pathology at Western Reserve University School of Medicine and author of published learned papers on: "Determination of Non-Paternity of Blood Groups." His qualifications as an expert serologist were not questioned by the complainant. He reported, in part, as follows: "The data on the Rh factor C, however, indicate that an exclusion of paternity is established on this basis. Both Hope Steiger and Bruce Gray are negative for the C factor and therefore lack this particular blood antigen. On the other hand baby Norma June Steiger is C-positive and therefore possesses this particular blood antigen. Since these blood factors can only be inherited from the parents and since both of these adults lack the C, then some other man than Bruce Gray must be the father of this child."

The existing Ohio statute does not make the result of blood grouping tests establishing an exclusion of paternity conclusive. Therefore, when scientific testimony regarding results of blood grouping tests and the testimony of lay persons as to facts conflict, as they do in this case, the jury or the trial court must determine the relative weight of both types of evidence. The question therefore arises, said the court, what weight and value shall the court give to uncontradicted blood grouping test evidence submitted by a qualified expert?

It is apparent, continued the court, that the testimony adduced from the parties and other lay persons in bastardy proceedings, by its very nature, may be susceptible to doubt and question. It is usually self-serving. The alleged intercourse between the woman and the putative father is almost always carried on clandestinely and secretly. Seldom if ever is there any reliable corroborating eye-witness testimony. Circumstantial evidence must be relied upon to a great extent. In other words, the testimony in such cases may be as reliable or as unreliable as the persons giving it. On the other hand an exclusion of paternity based on the blood groups represents a finding of a rather exact science and is not simply testimony of a lay witness or even the opinion of an expert. Blood-grouping test results are governed by the immutability of the scientific law of blood grouping and are based upon the scientific principle that the type of blood of a child is inherited from a combination of blood groups in the blood of its parents. In the instant case, continued the court, there being a positive C factor in the blood of the child, that blood factor must have been inherited from either the father or mother or both. Since the mother's blood lacks the C factor, the child must necessarily have inherited that factor from its father. But inasmuch as the defendant in this case also lacks the C factor, it follows as a matter of scientific certainty that some man other than the defendant fathered this child, and the defendant must be excluded as the parent.

Of course, the infallibility of the results of blood grouping tests may depend upon the skill employed in making them and may be subject to errors resulting from the lack of training of the serologist, the use of commercial sera, the failure to make proper counter tests, et cetera. But where it is shown that the person making the tests is qualified, that proper safeguards were drawn around the testing procedure, and that no discrepancies were found in the testing methods, a court is warranted in taking judicial notice of the correctness of such tests.

Enlightened judicial acceptance of the verdict of science, therefore, must result in the conclusion that where blood grouping tests in a bastardy proceeding prove nonpaternity, the court is not warranted in closing its mind to the conclusion that science declares is established—unless there is proof that the tests were not properly made, or that conditions did not exist to make the biological law operative.

The defendant was therefore found not guilty. *State* v. *Gray*, 145 N.E.(2d) 162 (Ohio, 1957)

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THE LEISURE CORNER

PUPPETS AND MARIONETTES

For centuries the puppet theater has occupied a prominent place in the world of amusement. Gordon Craig, the greatest modern authority on puppets, defines a puppet as a model of a man in motion. While puppets usually represent man, they also are models of animals, birds, fish, or any other creature or thing, real or imagined. A puppet must be moved by human contact, either directly or through strings or other mediums. If it is moved by machinery or clock work, it is not a puppet but becomes a mechanism or automaton. The puppet family is a great one in size, variety, and antiquity. In the National Museum in Washington, D. C., in the New York Museum of Natural History, in the Brooklyn and Chicago museums, a strange variety of puppets may be seen from all ends of the earth. Marionettes are worked by threads, cords, wires, or rods. They are usually swung from above, like those of the late Tony Sarg; but sometimes they are moved from below, not on the hand like fist puppets, but by rods. Some marionettes slide along in grooves. The usual, or dangling, type of marionette is generally slim, limber-jointed, and very agile. Fist puppets are also known as hand, finger, or mitten puppets. They consist simply of a small garment or mitten, to which are attached a head and hands. These are worn on the puppeteer's hand like a glove and are worked with his fingers.

Marionettes are far from a childish hobby. The poet Goethe surrounded himself with marionettes most of his life, and wrote of the marionettes and for them in the most charming manner. Few people realize that Socrates was an early forerunner of Edgar Bergen in his use of the puppet as a mouthpiece. Aristotle wrote that "by a mere pulling of strings the little figures could be made to use heads and hands, then eyes and shoulders and legs." Voltaire, who hated puppets at first, became a devotee when he found they could be made to assume responsibility for some of his more daring opinions. There is an endless list of marionette admirers, including Archimedes and Plato, Michelangelo and Goldoni, the composer Brahms, Shakespeare, Hans Christian Andersen, Molière, Anatole France, and George Bernard Shaw.

Marionettes are constructed of many different materials and fall into three types of categories, the naturalistic, the stylized, and the primitive. Since the naturalistic is the basis for all types, most people are accustomed to working with this type. The heads of most marionettes are composed of papier-mâché or plastic wood. The bodies are either cut from cloth, according to a pattern, then sewed, weighted and stuffed, or else constructed of wood, being jointed with various connecting materials such as cloth, leather, screw eyes, cord, or trunk fiber. Many stores sell ready-made marionettes, which are interesting and can be used to depict a variety of characters.

The particular aptitude that goes into making a good puppeteer is hard to define. It is known, however, that besides possessing manual dexterity, the puppeteer must have a certain objective as well as an extrovert personality. He should be able to lose himself completely in the identity of his puppet. He must therefore have a good sense of behavior, and, needless to say, a good sense of humor.

Beginners who have never handled puppets will often gingerly pull at every string just to see what action ensues. When the control is tilted from side to side, the puppet's head will move accordingly; when the control is dipped forward, the puppet bends forward. When the foot stick is held in advance of the control, tilting it from side to side will make the puppet walk.

With continual practice the operator will find that he is able to master the right string in the dark, without consciously looking for it. In this way he can make the entire marionette figure coordinate as a whole. In the process of practicing, a full-length mirror is very helpful. There you may stand, manipulating strings until the puppet will unerringly do your bidding and until your hand immediately obeys your own brain impulses as to the movement of strings.

It is almost impossible for the medical puppeteer not to compare the control strings of a marionette to the brain and nervous system. They are, in a sense, an extension of our own abilities through the action of strings. Until the strings are manipulated, a puppet is, after all, only a doll. Once a puppet is blessed with movement, it is difficult to regard it as a lifeless object without an individual personality. That is why many doctors who have worked with puppets for many years have never been able to destroy them.

The properties that are part and parcel of a marionette theater have all the charm of museum pieces. Parenthetically, it is just as much fun building puppet props as it is making the figures themselves. After you have made a few puppets and perhaps produced a show or two, you will appreciate the great antiquity of the marionette. Puppets of one sort or another have been part of the historical scene since the dawn of civilization. Tribes used puppets in their tribal ceremonies in prehistoric days. As man emerged from the Stone Age, he used small moving images, first as religious symbols, then for amusement. Some historians believe that puppets preceded living actors in the theater.

During the Middle Ages puppets owed their survival to the sanctuary of the Christian church. In order to bring reality to the teachings of Christ, monks made beautiful little figures depicting scenes from the Bible, carving them of wood, and richly clothing them. In Germany, where they were brought hundreds of years before by Roman conquerors, puppets attained a degree of perfection never before equaled in the Western World. In Italy, Michelangelo contributed suggestions and designs for hand puppets, dressing them in sack-like garments of brightly colored cloth. Pulcinella became a patron Saint, and wherever puppet showmen went, Pulcinella accompanied them with his ugly face and monstrous nose, features that always brought laughter to the audience. By the 18th century puppet shows were an accepted and important instrument of entertainment all over Europe and the British Isles, holding the same place in the hearts of the public as does television today.

Today, many hospitals regard marionettes as having considerable therapeutic value for both young and old patients. Perhaps this is why puppeteering has a bright forward look in the medical world.

MEDICAL FILM REVIEWS

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

Principles of Artificial Respiration: 16 mm., color, sound, showing time 27 minutes. Prepared by James L. Whittenberger, M.D., Benjamin Ferris Jr., M.D., and Jere Mead, M.D., Harvard School of Public Health. Produced in 1957 by Science Pictures Inc., under a grant from the National Foundation for Infantile Paralysis. Procurable on loan (service charge $1.00) from Motion Picture Library, American Medical Association, 535 North Dearborn St., Chicago 10.

The film shows the application of artificial respiration by a variety of techniques to a number of different human subjects in various situations, particularly industrial accidents and hospital conditions. These views are accompanied by animated diagrams to clarify the anatomy involved and to illustrate by physiological considerations the urgency of any situations involving asphyxia. In view of the speed of the narration and the complexity of the physiological ideas presented early in the film, even an audience of medical students and physicians should be prepared by some introductory remarks before they see it. If this film has a weakness, it is in the presentation of the preliminary argument about the relative importance of oxygen want as compared with carbon dioxide excess. This is undoubtedly intended to anticipate objections from physicians still influenced by the fear of acapnia inculcated so vehemently by the late Yandell Henderson. Because it is so complicated, it might well be replaced by the simple statement that over-ventilation rarely occurs and that the damage of over-enthusiastic application of artificial respiration (barring broken ribs) are nothing compared to the danger of oxygen lack resulting from delay or otherwise inadequate ventilation. This film deserves the highest praise, and it is probably best adapted to audiences of medical students, nurses, and physicians who need to be brought up to date on the most recent developments of artificial respiration, namely, the back pressure arm lift method and the mouth to mouth or mouth to nose technique.

The following films were produced in 1957 by Churchill-Wexler Film Productions, Los Angeles, for the American Heart Association and are procurable on loan (service charge $1.00 each) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

Coronary Heart Disease: 16 mm., color, sound, showing time 6 minutes.

In this film, an animated demonstration of coronary arteries, their location and function, serves as an introduction to a discussion of hardening of the arteries and angina pectoris, or coronary insufficiency. The animation continues, showing a typical damaged area and the ability of other arteries to eventually feed this area. Heart attack, or coronary thrombosis, is also illustrated, and the film ends with a brief discussion on the satisfactory recovery of many patients.

High Blood Pressure: 16 mm., color, sound, showing time 6 minutes.

This film begins with an animated introduction to arteries, arterioles, and capillaries. The pumping action of the heart is demonstrated in connection with apparatus for measuring blood pressure. High blood pressure, or hypertension, is then discussed and illustrated in detail. A typical patient with hypertension is shown to emphasize that most patients suffering from this condition can lead normal lives under the care and guidance of their physicians.

Strokes: 16 mm., color, sound, showing time 6 minutes.

With the use of schematic animation, the nerve cells in the brain and their pathways to other parts of the body are shown. The blood supply to the brain which brings food and oxygen to the nerve cells is also demonstrated. Interruption of this blood supply can be caused by hardening of the arteries (atherosclerosis), clot formation, or a break in an artery usually associated with hypertension. The result, a stroke, is illustrated in detail. A few scenes of early rehabilitation of patients with strokes are shown.

These three excellent films could be used separately or together for any lay-group instruction. They are scientifically accurate and are recommended for science classes in junior high and high schools and also for physicians who are called on to speak to lay groups on the subject of heart disease.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

A Study of the Etiological Factors in Cancer of the Mouth. E. L. Wynder, I. J. Bross and R. M. Feldman. Cancer 10:1300-1323 (Nov.-Dec.) 1957 [Philadelphia].

The authors report on 659 patients, 543 men and 116 women, with cancer of the oral cavity who were studied in an attempt to determine the influence that environmental factors may have on the development of cancer of the oral cavity and to determine whether these factors could account for differences in the incidence pattern for this type of cancer. For the study of possible causative factors, the patients with cancer of the oral cavity were matched with 439 controls, including patients with benign diseases of head, neck, and thorax, lymphomas, and cancers of the lower gastrointestinal tract. The incidence pattern of cancer of the oral cavity showed a predominance of men affected with this disease. It showed a leveling off and perhaps even a slight decrease of the incidence in men at the present time, while a small increase was noted among women.

Smoking was an important factor in the development of cancer of the oral cavity. Only 3% of the 543 men with cancer of the oral cavity never smoked, in contrast to 10% of the controls, but 29% were excessive smokers as compared with 17% of the controls. In contrast to studies on cancer of the lung in which cigar and pipe smoking were found to play a minimal role, cigar and pipe smoking increased the risk for cancer of the oral cavity more than cigarette smoking did. Thirty-four per cent of the patients with cancer of the oral cavity were cigar and/or pipe smokers, in contrast to 21% of the controls and 7% of patients with cancer of the lung. Tobacco chewing was of some, although lesser, importance in the development of cancer of the oral cavity. Seventeen per cent of the patients were tobacco chewers, in contrast to 9% of the controls. In women also cigarette smoking represented a factor in the development of cancer of the mouth. There were twice as many nonsmokers among the controls than among the patients, and there were 3 times as many chain smokers among women with cancer of the oral cavity than among the controls.

Alcohol consumption, particularly whiskey consumption, represented an important factor in the development of cancer of the oral cavity. The main effect was on patients who drank 7 oz. of whiskey or more a day. Thirty-three per cent of the male patients with cancer of the oral cavity drank this amount, as compared with 12% of the controls. Syphilis was of significance in the development of cancer of the lip and the anterior two-thirds of the tongue. It is not clear whether this relation is a result of syphilitic glossitis or whether it is related to the arsenic therapy that most of the patients received. Trauma and dental irritation were not significant factors in the development of cancer of the mouth. Edentia was more common among patients with cancer of the mouth; particularly in women. Pregnancy had a significant influence on edentia. The fact that no major change in the incidence of cancer of the oral cavity has been seen in men is consistent with the data presented. The increase in tobacco use has been primarily an increase in cigarette consumption. This would influence an increase in the incidence of cancer of the lung but not that of cancer of the oral cavity in which cigarettes appear to play a lesser role than cigars and pipes. For the latter 2 types of smoking there has been a slight decrease in consumption. The amount of tobacco chewed has also declined during recent years. The slight increase in cancer of the oral cavity in women is compatible with the fact that few women have been smoking more than 20 years. The factors of tobacco and alcohol consumption are, therefore, consistent with the incidence rate for cancer of the oral cavity as it exists in the United States today. For cancer of the lip, exposure to sunlight is of additional causative significance. Since tobacco and alcohol consumption are to be considered the major extrinsic factors influencing the development of cancer of the oral cavity, it is estimated that the rates for men and women would be similar if either the exposure of women to these agents would be increased or the exposure of men decreased. This would mean that if the exposure were, in fact, decreased the incidence of cancer of the oral cavity in men would drop from 19 to 5 per 100,000. In view of the fact that at least some of the cases of cancer in women

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The place of publication of the periodicals appears in brackets preceding each abstract.

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are also influenced by tobacco and alcohol, the actual incidence rate might be even lower. These data indicate that about 4 out of 5 cases of cancer of the oral cavity in American men are preventable.

Digitalis Intoxication: A Review and Report of Forty Cases, with Emphasis on Etiology. M. W. Shrager. A. M. A. Arch. Int. Med. 100:881-893 (Dec.) 1957 [Chicago].

The author reviews observations on 40 selected patients with digitalis intoxication. Age was not found to be a barrier to effective therapeutic exhibition of digitalis. The type of heart disease was not significant, except that acute myocardial infarction seemed to predispose to development of toxicity in 3 patients. Digitoxin produced severer toxicity with fewer warning gastrointestinal symptoms than did digoxin. Nausea and vomiting were the most prominent symptoms, but anorexia was often missed as an early symptom of intoxication. "Neurologic" symptoms were a common manifestation of digitalis intoxication, but these were usually accompanied also by gastrointestinal symptoms. Ninety-three per cent of the patients had pulse irregularities; bradycardia was found in 25%. Arrhythmias were demonstrable by electrocardiography in 95% of the cases, but auricular fibrillation was attributable to digitalis intoxication in only 3 of 14 cases reported with this arrhythmia and was accompanied by other arrhythmias in 11 of these 14 cases. Bigeminy was present in 25% of cases of intoxication. Six patients with refractory heart failure are reported, 5 of whom improved with the withdrawal of digitalis. Failure to attribute advancing congestive heart failure to digitalis intoxication may be a serious error. When clinical signs and symptoms are compatible with both congestive heart failure and digitalis intoxication and if the congestive failure has not previously responded to adequate digitalis dosage, benefit will often be obtained by stopping or reducing rather than by increasing dosage or by exhibiting potassium or procainamide.

In 80% of the patients the digitalis intoxication could have been prevented by the attending physician, and 88% of these could be attributed to errors in dosage. A common error, responsible for 9 cases (23%) of toxicity here reported, was an attempt to control intractable failure by exhibiting high-maintenance doses or by adding frequent small supplementary doses to an already adequate maintenance dose. If dosage is to be increased in such cases, electrocardiograms should be made frequently and the patient should be observed in a hospital in order to spot early signs or symptoms of intoxication. Small increases of dosage are especially hazardous in patients with any of the well-known limitations to digitalis therapy, namely, poor myocardial status, electrolyte imbalance due to diuresis and congestive failure, acute myocardial infarction, pulmonary embolism, severe kidney disease (especially with oliguria), and advanced liver disease. Failure to follow patients who were receiving a normal maintenance dose of digitalis preparations, inadequate individualization of these "normal" doses, and especially failure to reevaluate dosage on the basis of advancing congestive failure and other criteria which may predispose to digitalis intoxication were common errors. The potential gravity of the syndrome of digitalis intoxication and the results of therapy with oral potassium and discontinuation of digitalis are evaluated. In a small number of cases the average time for disappearance of symptoms or signs of intoxication due to digoxin was 2-3 days and with digitoxin, 9 to 11 days.

Auricular Fibrillation: Report on a Study of a Familial Tendency, 1920-1956. W. L. Gould. A. M. A. Arch. Int. Med. 100:916-926 (Dec.) 1957 [Chicago].

The record of a continuing 36-year study of a familial tendency toward auricular fibrillation is presented. A total of 113 persons in 5 generations of one family were studied. Of 41 members of this family who lived to the age of 40 years, there were 21 with fibrillation. The condition became perpetual in 9 of the 22 patients who reached the 7th decade of life. Many of those just entering their 5th or 6th decade are now developing fibrillation. One person had a fibrillation for 38 years with no signs of decompensation at any time. This patient had great difficulty in obtaining a diagnosis. The cause of his attacks of weakness, dizziness, and faintness could not be ascertained. Even during a 10-day period of observation and testing in a hospital no heart irregularity was noted. Only 2 years later, when the attacks became more pronounced, was fibrillation detected. Eleven years after the original attack it became perpetual.

Treatment varies from patient to patient. Persons with familial auricular fibrillation should not be treated for cardiac failure, since this type of auricular fibrillation does not even predispose the patient to cardiac failure. Some patients have fibrillation without knowing it, while others are aware of them. One patient who frequently experienced fibrillation found that if he stopped taking his pulse too regularly he experienced fibrillation less often. When the fibrillation is not abated by ordinary postural means, intestinal evacuation for any gaseous distention, or other methods, barbiturates are the drugs of choice. They appear to be far more beneficial than either digitalis or quinidine. Glyceryl trinitrate (nitroglycerin) was found to be of no use in treating these patients. Patients should be kept in good general health and avoid excesses, such as overeating and overfatigue, when they know that this may bring about an attack. Allergic manifestations should be avoided. The prognosis for patients

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with auricular fibrillation is that they will live normal healthy lives. Even with perpetual fibrillation, most lived to old age. Major dangers of this condition are misdiagnosis resulting in enforced bed rest or diagnosis which leads to overconcern and anxiety on the part of the patient.

Unheralded Pulmonary Embolism. H. Cohen and J. J. Daley. Brit. M. J. 2:1209-1212 (Nov. 23) 1957 [London].

Pulmonary embolism occurring in patients who appear to be fit and active and who have no signs of venous thrombosis has been termed "unheralded pulmonary embolism." Pulmonary embolism is a common disease which accounts for 2 to 3% of all deaths in hospitals and is suspected in patients who have acute chest pains either postoperatively or after prolonged bed rest. Ten cases of pulmonary embolism are described. None of the patients had signs of peripheral venous thrombosis when first seen, and 8 had been active until they developed chest symptoms, 2 having been confined to bed for only a week. Almost all of the patients had recurrent attacks of pleurisy which did not respond to treatment with antibiotics, although temporary relief was forthcoming after each acute attack and was attributed to the antibiotic given at that time. A prominent feature was the absence of purulent sputum. The patients treated with anticoagulants recovered and have not developed cor pulmonale. Although pulmonary embolism is clinically indistinguishable from pulmonary artery thrombosis, the treatment for both conditions is the same and the important concept is that of recognition of the syndrome complex.

The Prevention of Myocardial Infarction. B. Manchester. A. M. A. Arch. Int. Med. 100:959-964 (Dec.) 1957 [Chicago].

The author presents his experience with continuous long-term anticoagulant therapy for the prevention of subsequent coronary thrombosis and cardiac infarction. The observations were made over a period of 1 to 10 years in 712 patients with 1 or more myocardial infarctions prior to this study. The incidence of subsequent myocardial infarction, congestive heart failure, angina pectoris, thromboembolic complications, and the survival by patient-year were observed in control, anticoagulant, and "untreated" groups. Alternate patients received an oral anticoagulant and ascorbic acid, while the control received 250 mg. daily of a placebo of ascorbic acid. Except for oral anticoagulants, bishydroxycoumarin (Dicumarol), or acenocoumarin (Sintrom), both groups received the same medical care, dietary regimen, and digitalis, diuretics, and/or sedatives as required. After 10 years there remained 404 patients who had cooperated and continued uninterruptedly the medical regimen outlined. Two hundred four continued to take oral anticoagulants (bishydroxycoumarin or acenocoumarin) from 1 to 10 years, and 200 were maintained with the placebo of ascorbic acid. Of the remaining 308 there are 157 available for follow-up and comparison; they are referred to as the "untreated" group and serve as another control.

Subsequent myocardial infarction occurred in 29 patients of the anticoagulant group (14.2%), and 6 of these patients died; in 68 (34%) of the control group, and 36 of these patients died; and in 63 (40.1%) of the untreated group, and 35 of these patients died. Thus, continuous long-term anticoagulant therapy proved effective in preventing subsequent myocardial infarction and increased patient-year survival. Such therapy is practical, feasible, and economical. The use of a simple capillary blood prothrombin test employed in the present series made the management inexpensive and practical. The author concludes that continuous long-term anticoagulant therapy is a significant advance in the prevention of subsequent coronary thrombosis. Such therapy may prolong life and productivity. For the man who associates "heart attacks" with sudden death, abbreviated life span, or invalidism, this report provides a more optimistic outlook for the future.

The Value of Continuous (1 to 10 Years) Long-Term Anticoagulant Therapy. B. Manchester. Ann. Int. Med. 47:1202-1209 (Dec.) 1957 [Lancaster, Pa.].

The author reports on the value of continuous long-term anticoagulant therapy, observed from 1 to 10 years in 712 patients with one or more myocardial infarctions. The incidence of infarction, mortality, congestive heart failure, angina pectoris, thromboembolic complications, and survival by patient-years was observed in the control and the anticoagulant groups. Patients were first seen and followed during an acute episode of myocardial infarction, confirmed clinically and electrocardiographically. Alternate patients received an orally administered anticoagulant and ascorbic acid, while the controls received a placebo of ascorbic acid, 250 mg. daily. The result of anticoagulant therapy in acute myocardial infarction in the first 500 patients has been reported previously. After 10 years there remained 404 patients who had cooperated and continued the medical regimen uninterruptedly. Two hundred four have continued the oral therapy with anticoagulants (Dicumarol or Sintrom) for from 1 to 10 years, and 200 have received the placebo of ascorbic acid. Included in the control group are 23 patients who did not wish to remain on anticoagulant therapy after recovery from the acute infarction.

The standards of cooperation, the number of visits required, and the criteria of selection were strictly adhered to in both groups. The therapy

proved practical, feasible, and economical. The use of a simple capillary blood prothrombin test made the management inexpensive and practical. The incidence of subsequent infarction was 3 times greater in the control group; the mortality rate was 8 times more in the control than in the anticoagulant group. Continuous long-term anticoagulant therapy is a significant advance in the prevention of subsequent coronary thrombosis. The data provide evidence that such therapy may prolong life and productivity.

Myxoma of the Left Auricle. J. C. Harvey. Ann. Int. Med. 47:1067-1081 (Dec.) 1957 [Lancaster, Pa.].

Myxoma of the left atrium usually arises from the intra-atrial septum in the region of the fossa ovalis. It is attached to the wall by a pedicle of varying length. This form of tumor is of varying sizes, with smooth, polypoid surfaces. Some myxomas may have villous processes. They are composed of loose myxomatous tissue intertwined with elastic fibers and are relatively avascular. Necrosis, hemorrhage, and secondary organization within the mass are common. On occasion, bits of tissue break off from the surface of the tumor, forming emboli. There is controversy as to whether these tumors are organized thrombi or actual neoplasms. Mechanically, these tumors in the left atrium offer obstruction to the flow of blood through the atrium or through the mitral valve.

The author presents 5 patients with myxoma of the left atrium observed on the medical service of the Johns Hopkins Hospital. The patients had symptoms and physical signs compatible with rheumatic heart disease and mitral valvulitis. Arthralgias, breathlessness, and palpitations were prominent. There were loud, snapping first mitral sounds and apical systolic and diastolic murmurs. All presented findings indicative of increased pulmonary pressure. Each patient had an accentuated second pulmonic sound. In all patients except one the right ventricle was enlarged, as observed by percussion and on roentgenologic examination. The electrocardiogram in each instance showed right axis deviation.

A significant difference exists between the obstruction to the left atrial outflow produced by a myxoma and that produced by a stenotic mitral valve. Some freedom of movement is permitted the tumor within the atrial cavity by its stalk-like attachment to the interatrial septum. Thus, the symptoms and the auscultatory signs will vary with body position. The patients all reported that symptoms first appeared when they stooped or bent forward. The onset of symptoms is sudden. Heart failure is progressive. Syncope is frequent. Embolic phenomena commonly occur in the systemic, cerebral, or coronary circulations. Intermittent fever, petechiae, and changing cardiac murmurs often suggest erroneously the diagnosis of bacterial endocarditis. Laboratory aids are of little value in making a diagnosis. The lesion, if untreated, leads inevitably to death, but recent advances in cardiac surgery have made possible the successful removal of these tumors.

Hypercholesterolemia, Xanthomatosis and Coronary Insufficiency. G. Welin and K. Cramér. Nord. med. 57:765-768 (May 30) 1957 (In Swedish) [Stockholm].

During a 26-month period 58 cases of essential hypercholesterolemia, in 24 men and 34 women, were diagnosed among patients seeking medical aid because of heart disease or diffuse precordial pain. Tendon xanthomas were found in 32 patients, mainly in the extensor tendons of the fingers, and arcus corneae was seen in 26 patients, as a rule in men with severe heart disease. There was a positive family history of coronary heart disease in 22 cases. Significant endocrine factors, especially steroid metabolism, which is unusual in women before the menopause, and metabolism of thyroid hormone, play an essential part in maintaining a pathologically increased serum cholesterol. Nineteen men had had infarction or had so grave angina pectoris that they were unable to work. Two patients died suddenly from infarction; 1 patient died from cerebral thrombosis. The prognosis is unfavorable.

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SURGERY

Intrapericardial Bronchogenic Cysts: Report of Two Cases and Probable Embryologic Explanation. C. H. Dabbs, R. Berg Jr. and E. C. Peirce II. J. Thoracic Surg. 34:718-735 (Dec.) 1957 [St. Louis].

Aside from the usual paratracheal, carinal, hilar, or paraesophageal location, cystic tumors of bronchial origin have been reported in association with vertebral bodies, in the presternal area, and intrapericardially. Bronchogenic cysts or "teratomas" are unusual within the pericardium. From the literature and their own observation, the authors have collected 20 cases of intrapericardial bronchogenic cysts, to which they add 2 new cases. The patients were women, aged 42 and 20 respectively. Both tumors were removed successfully, although they were quite large, the first having a broad aortic attachment measuring approximately 4 by 2.5 cm. The tumor in the second patient was a partially calcified mass, weighing 650 Gm. with a diameter of 10 cm. The correct diagnosis was made preoperatively in 1 after clinical study which included angiocardiography. Although a few of the tumors reported in the literature are clearly teratomas, most of them resemble closely the tumors which the authors report and probably should be classified as bronchogenic cysts. The predominating elements are cystic spaces lined with respiratory epithelium containing mucous glands, cartilaginous

plates, and lymphoid follicles. Squamous epithelium and tissue derived from gastrointestinal primordia may also be present.

The following embryologic explanation for the bronchogenic cysts within the pericardium is advanced. During the 28-day to 34-day period the "lung buds" are in close contact with the dorsal mesocardium and heart tube. It appears logical that cells having respiratory (and gastrointestinal) potential may become displaced, develop in juxtaposition to the aorta and superior vena cava, and become sealed within the pericardium by fusion of the pleuropericardial fold. The few cases which are strikingly similar grossly but which contain tissue clearly of ectodermal origin must be diagnosed as teratoma. The authors have no adequate explanation for their similarity nor their occurrence here, unless it be by the same mechanism, with metaplasia of the primordial cells. The x-ray configuration and the deformity produced on angiocardiography appears characteristic. Surgical attack without proper knowledge of the intimate association of these tumors with the cardiac chambers and the great vessels may be disastrous. Exact diagnosis and precise localization in relation to the anatomy of the heart preoperatively should lead to successful removal in most instances.

The Endocrine Dependency of Certain Thyroid Cancers and the Danger That Hypothyroidism May Stimulate Their Growth. G. Crile Jr. Cancer **10:** 1119-1137 (Nov.-Dec.) 1957 [Philadelphia].

Since June, 1953, all patients operated on at the Cleveland Clinic for cancer of the thyroid have been given 2-3 grains of desiccated thyroid daily, starting as soon as the diagnosis was established and continuing indefinitely. It is too early to evaluate the results of this therapy, but during the first 2½ years 50 patients with papillary carcinoma and 5 with encapsulated angioinvasive carcinomas were operated on, and the cases of 17 of them, 4 men and 7 women between 17 and 65 years of age and 5 boys and 1 girl between 5 and 9 years of age, are reported in detail. In all but 2 of these patients the entire primary tumor and its grossly evident cervical metastases were removed. It is now 1-3½ years after operation, and there are only 2 patients taking thyroid as prescribed who show any persistence or recurrence of their tumors. A tiny operable recurrent tumor developed in the scar of 1 of the 2 patients, whose primary rapidly growing tumor could not be excised completely. The other had palpable persistence of the primary tumor and a lymph-node metastasis, but neither of these had enlarged. It is too early for these figures to be more than suggestive, but in the past the recurrence rate of papillary carcinoma was 18% and most of these recurrences appeared in the first 2 or 3 years. It is already apparent that the expected number of recurrences did not develop in the patients taking thyroid. The arrest or regression of all but 2 of the papillary cancers in this series and the striking retardation of growth in these 2 cases suggest that thyroid feeding often induces a remission of differentiated thyroid cancers.

Since data both from laboratory and clinic indicate that thyroid-stimulating hormone (TSH) stimulates the growth of many thyroid cancers, any form of treatment that removes the thyroid or impairs the function of the thyroid may increase the output of TSH and accelerate the growth of metastases from a thyroid cancer. Conversely, feeding thyroid may inhibit the growth of dependent thyroid cancers. Two illustrative cases, 1 in a 27-year-old woman and 1 in a 59-year-old man are reported. In the woman, there was steady spread of proved pulmonary metastases of papillary carcinoma of the thyroid after total thyroidectomy and treatment with methimazole (Tapazole) and radioactive iodine (I^{131}). There was no demonstrable growth of the metastases before treatment with I^{131}, providing suggestive evidence that the rapid spread was the result of induced hypothyroidism. Treatment with adequate doses of desiccated thyroid resulted in rapid clearing of the lungs and disappearance of dyspnea. The regression was directly attributable to the treatment with thyroid. In the man, low-grade papillary cancer was treated through a natural history of 15 years, during which time it grew more malignant both histologically and clinically. After thyroidectomy and radium therapy it grew more rapidly and became an undifferentiated carcinoma. Suppression of the normal function of thyroid by thyroidectomy, by administration of I^{131}, or by administration of thiouracil subjects any residual thyroid tumor to prolonged stimulation by TSH. Instead of increasing the differentiation and function of such a tumor, stimulation by TSH ultimately produces the opposite effect and may transform a differentiated, slowly growing, dependent cancer into a rapidly growing autonomous, functionless, and wildly metastasizing cancer. To prevent this, all patients with cancer of the thyroid should receive adequate thyroid hormone. Hypothyroidism should never be allowed to persist. Most inoperable thyroid cancers should not be treated by I^{131} until they have been given a trial treatment with desiccated thyroid.

Supernumerary Intrathoracic Rib: A Case Report. G. E. Plum, A. B. Hayles, A. J. Bruwer and O. T. Clagett. J. Thoracic Surg. **34:**800-803 (Dec.) 1957 [St. Louis].

The 9-year-old girl whose history is presented was brought to the Mayo Clinic with a suggested diagnosis of "lung tumor" on the basis of a roentgenogram made by a mobile unit. A well-defined area of increased density had been seen adjacent

to the hilus of the right lung and extending from the level of the anterior end of the second rib to the right cardiophrenic angle. Surgical exploration had been advised, whereupon the patient had come to the Mayo Clinic for further examination. The girl had no symptoms referable to the thorax. In roentgenograms of the thorax, made in posteroanterior, lateral, and oblique projections, there was a shadow with a convex lateral border lying far posteriorly on the thoracic wall. It appeared to originate near the right lateral border of the 6th thoracic vertebal body and extended downward posteriorly to the 9th intercostal space. Twelve pairs of normal ribs were present.

Diagnoses that were considered included anomalous blood vessel, intrathoracic cyst, lipoma, and duplication of the esophagus. Exploratory thoracotomy revealed an anomalous supernumerary rib that lay within the thoracic cage but outside the parietal pleura. The rib originated from the right lateral margin of the 6th thoracic vertebra, anterior to and between the vertebral articulations of the 6th and 7th ribs, and extended downward posteriorly to about the 10th rib. It was completely removed without difficulty. The authors have no criteria to offer in making a roentgenologic diagnosis of supernumerary rib. In the case presented, the roentgenologic identity apparently was masked by the pleural reflections from the rib; these imparted a "soft" cyst-like appearance. Possibly use of tomography would have clarified the nature of the shadow.

Esophageal Hiatus Hernia of the Diaphragm: An Analysis of Surgical Results. G. H. Humphreys II, J. M. Ferrer Jr. and P. D. Wiedel. J. Thoracic Surg. 34:749-767 (Dec.) 1957 [St. Louis].

The authors review the present status of knowledge of the anatomy, physiology, and symptomatology of hernias through the esophageal hiatus of the diaphragm and the current classification of such hernias. A method for repair of uncomplicated sliding hiatal hernia which has been used for 8 years is described. This method takes account of the fact that the chief problem in this type of hernia is a weakening and widening of the posteromedial crural fibers, allowing the cardia to slide upward into the mediastinum. Since the symptoms are primarily due to the resulting incompetence of the cardia, the main problem is to return the cardia to its normal position, hold it there, restore the esophagogastric angle, and bring together the posterior fibers of the right crus, reducing the hiatus to normal size. Since there is no true sac, there is no need to enter the peritoneal cavity. Recurrence should best be prevented by establishing firm union between the wall of the stomach all around the cardia and the adjacent under-surface of the diaphragm above and medial to the peritoneal reflection. Tight closure of the hiatus around the esophagus is unnecessary, may cause dysphagia, and is ineffectual, since sutures in the muscular wall of the esophagus do not hold well. When the herniated stomach has been completely freed of its attachments in the mediastinum, it can be lifted forward and medially to expose the acute angle of the posterior end of the esophageal hiatus, which is formed by overlapping sheets of the right crural fibers. This angle must be partially closed, and at the same time the esophagogastric junction must be fixed below it.

The long-term results, from 2 to 9 years after operation in a series of 97 operations in 96 patients with hiatal hernia of various types, have been reviewed. A variety of procedures were used by 28 surgeons in 1 hospital. The results show that the great majority of hiatal hernias are of the sliding type. There were 87 sliding, 6 paraesophageal, and 2 esophagoaortal hernias. One infant is included, with an intrathoracic stomach presumably due to congenital failure of descent. The operation described was carried out in 24 of the 88 operations for sliding hernia. Results were good in 83%. Other transthoracic methods were used in 52 operations with good results in 42%. Transabdominal operations were reserved for complicated cases and were done 8 times, with only 2 good results. In 4 patients the hernia was not repaired at operation. One of these and 2 other patients with sliding hernia died as a result of the operation, none of them following the described procedure. Paraesophageal and esophagoaortal hernias require more complex operations, though the same principles apply. Three of the 6 patients with paraesophageal hernias were operated on for acute incarceration, 2 with good and 1 with fair results. Only 1 of the elective repairs ended with a good result. It is concluded that the method described is effective in a high proportion of uncomplicated cases of sliding hernia and that early operation is therefore indicated.

Elevation of Blood Ammonium in Hemorrhagic Shock. J. S. Horsley, J. J. De Cosse, M. Hood and others. Ann. Surg. 146:949-956 (Dec.) 1957 [Philadelphia].

The authors performed experiments in dogs in an attempt to correlate alterations in blood ammonium, ph, carbon dioxide, carbon dioxide pressure, and potassium with the electrocardiographic changes in 11 of 16 animals subjected to hemorrhagic shock irreversible by transfusion. The animals were bled from the right femoral artery into a vacuum-sealed bottle containing heparin. The bleeding was continued at the rate of about 50 cc. per minute until the mean arterial pressure was reduced to 50 mm. Hg. Blood pressure was maintained for 90 minutes at this level and then decreased to 30 mm. Hg. for

30 minutes by further bleeding. After this, transfusion of all withdrawn blood was carried out at a rate of about 50 cc. per minute into the right femoral vein. Three dogs survived, and of the 8 dogs which died as a result of this procedure, 3 died immediately, despite transfusion, and 5 lived from 1 to 7 hours after completion of the transfusion. There was a definite change in the blood electrolyte picture in all animals. There was a drop in total carbon dioxide and pH with a rise in potassium and ammonium levels. Marked changes in blood pH and ammonium levels occurred simultaneously with marked electrocardiographic changes. The eventual survival of the dog subjected to hemorrhagic shock could be predicted by these changes in blood ammonium and pH and associated electricardiographic alterations. The dogs that died showed a marked increase in osmotic pressure which could not be accounted for by alterations in electrolytes. In addition to the 11 dogs studied, 5 dogs were treated with monosodium glutamate in an attempt to protect against the elevation in ammonium level. These dogs were subjected to the same procedure of hemorrhagic shock as the preceding group. Monosodium glutamate protected these animals from marked changes in blood ammonium levels and electrocardiographic alterations and permitted more blood to be withdrawn before shock levels were attained. Nevertheless, the administration of this agent did not prevent death, and all 5 animals died.

The results of these experiments confirmed the occurrence of elevation of the blood ammonium level in hemorrhagic shock. That the liver is essential to the handling of ammonium cannot be denied. In hemorrhagic shock, there is not only decreased hepatic blood flow but also increased concentration of ammonium in the blood which reaches the liver. The liver is unable to reduce the concentration adequately, and under such circumstances the blood ammonium level rises as the dog goes deeper into shock. It is suspected that both metabolic acidosis and the elevated ammonium and potassium levels may well have caused the electrocardiographic alterations which heralded the irreversibility of the hemorrhagic shock in the dogs. It was noted that, unless corrected, these changes quickly led to marked bradycardia, ventricular fibrillation, and death.

PEDIATRICS

Immunologic Studies in Congenital Agammaglobulinemia With Emphasis on Delayed Hypersensitivity. H. M. Porter. Pediatrics **20**:958-965 (Dec.) 1957 [Springfield, Ill.].

The genetic background of 2 first cousins (boys) with congenital agammaglobulinemia and immunological studies in 1 of these patients are reported. The main characteristics of the disease are repeated bacterial infections starting in childhood, serum gamma globulin level below 30 mg. per 100 ml. in the presence of normal total serum protein level, the inability to produce circulating antibodies, the absence of plasma cells from the bone marrow and of isohemagglutinins from the blood, and protection from infection by injection of pooled gamma globulin. The family history of the cousins shows that numerous male children died in infancy, whereas all females survived to adult life. All living members of the family were tested for concentration of gamma globulin in the serum, and only 2 who had agammaglobulinemia had abnormal values. The appearance of the disease in male members of this family only is characteristic of the congenital form of agammaglobulinemia. This family history provides further evidence that this disease is a sex-linked recessive trait.

The immunological studies show that there is no defect in the production of the delayed type of skin sensitivity despite the patient's inability to form circulating antibodies. The delayed type of hypersensitivity was normally produced in response to antigenic stimuli, but circulating antibodies of the gamma globulin fraction of the serum were not. It is postulated that delayed hypersensitivity is responsible for the apparent immunity developed against measles and chicken pox. The tuberculin response is independent of gamma globulin in the serum.

Cat Scratch Disease as a Cause of the Oculoglandular Syndrome of Parinaud. A. M. Margileth. Pediatrics **20**:1000-1005 (Dec.) 1957 [Springfield, Ill.].

Ten children with cat scratch disease were observed in the author's pediatric service in the course of 3 years. Five of these children had the common glandular form involving the axillary, epitrochlear, or inguinal lymph nodes. The case of the 6th patient was unusual in that the primary lesion was in the midline at the base of the neck posteriorly, followed in 1 week by involvement of the trapezius lymph nodes which remained enlarged for 4 months. These patients recovered uneventfully in several weeks or months. The remaining 4 children, whose case histories form the basis of this report, were also unusual in that the primary lesion was noted in the conjunctiva, and in each instance this was followed by preauricular lymph node enlargement. The first of the 4 children was referred to the pediatric clinic for biopsy of the tumor in the parotid area. Because of the history of contact with cats and the author's recent experience with the glandular form of cat scratch disease, studies were performed to disprove bacterial infection, tuberculosis, tularemia, brucellosis, and syphilis. The skin test using cat scratch disease antigen was positive.

The other 3 children also exhibited lesions of the eye and enlargement of the regional lymph nodes. One child already had had excision of the conjunctival granuloma, but the other 2 had not, and histological examination was possible. One lesion demonstrated a typical microabscess similar to those described by Marshall in the regional lymph nodes of cases of cat scratch disease. A diagnosis was established in each child with use of cat scratch disease antigen. The author stresses that, in patients with periauricular adenopathy, not only should the eyes be thoroughly examined but skin tests should be made with cat scratch disease antigen. Surgical excision of the primary ocular lesion appears to shorten the course of the disease. Antibiotic therapy was ineffective in comparison with excision of the ocular granuloma.

Unilateral True Hermaphroditism: Two Cases With Sex-Chromatin Positive Cellular Pattern. I. M. Rosenthal, J. H. Kiefer, E. McGrew and I. P. Bronstein. Pediatrics **20**:1006-1018 (Dec.) 1957 [Springfield, Ill.].

The discovery of the patterns of chromatin in human somatic cells characteristic of normal males and normal females by Barr has been followed by the investigation of the distribution of chromatin in the various types of human sexual aberration. The authors describe observations of 2 young children with true hermaphroditism. Each had an ovotestis on 1 side and an ovary on the other. True hermaphrodites may be either sex-chromatin positive or sex-chromatin negative, as determined by biopsy of the skin. Each of these children was sex-chromatin positive, and thus the genetic sex of each was presumably female. Female sex was assigned to each child after careful consideration of all factors. In each case appropriate surgery was performed on the gonads and genitalia. In order to obtain optimal psychosexual development, patients with intersexuality should be studied diagnostically in infancy so that definitive unequivocal assignment of sex can be made before gender role is established.

Acute Lower-Respiratory Infections in Childhood. B. Morrison, D. Bass, J. A. Davis and others. Lancet **2**:1077-1082 (Nov. 30) 1957 [London].

The 191 cases of acute respiratory illness severe enough to warrant admission to hospital and representing consecutive admissions were divided into 4 clinical groups according to the dominant clinical characteristics: (1) segmental pneumonia (46); (2) bronchopneumonia (55); (3) bronchiolitis (51); and (4) simple bronchitis, tracheobronchitis, and laryngotracheitis (39). A highly significant correlation between the age of the child and the predominant clinical picture was found; there was an excess of bronchiolitis among the infants (aged 0-1 year), of bronchopneumonia among the toddlers (aged 1-4 years), and of segmental pneumonia among the older children (aged 5 years or more). The isolation rate of pathogens depends to some extent on the age of the infant, being higher in the infants and older children than in the toddlers. Despite the fact that a potential pathogen was grown in almost every instance of infantile bronchiolitis, infants aged less than 1 year showed a specific response to antimicrobial therapy in only 31% of the cases, in contrast to the response in 86% of the babies with segmental pneumonia and 59% of those with bronchopneumonia; this finding is compatible with the tenet that bronchiolitis is essentially a virus disease, although clinical evidence would seem to indicate that there is a nonbacterial infection which runs its course and that the bacterial infection is secondary to the virus infection. The proportion of infants aged less than 1 year with bronchiolitis having polymorphonuclear cell counts greater than 5,000 per cubic millimeter is considerably less than that of infants of the same age suffering predominantly from segmental pneumonia or bronchopneumonia. Anemia, which was defined as a hemoglobin level of less than 11 Gm. per 100 cc. of blood, was present in nearly one-third of the children and in nearly half of those aged less than 2 years. The association between anemia and acute respiratory infection is uncertain, since anemia is found quite commonly in young children. The findings suggest that, in this age group, a primary virus infection often produces a mild illness which is succeeded by secondary bacterial pneumonia, possibly after partial bronchial obstruction, in which event chemotherapy may be of secondary importance to oxygen therapy in infants with severe hypoxia associated with obstructive bronchiolitis.

An Epidemic Among Swedish Children Caused by Adenovirus Type 3. L. Kjellen, B. Zetterbert and A. Svedmyr. Acta paediat. **46**:561-568 (Nov.) 1957 (In English) [Uppsala, Sweden].

The investigations described were started about 1 month after the occurrence of the first cases with symptoms typical of "pharyngoconjunctival fever"—upper respiratory disease, conjunctivitis, and diarrhea. The local medical authorities in the 2 neighboring communities in central Sweden by this time knew of at least 100 cases, predominantly among children. One of the authors visited the epidemic area and personally examined some of the patients with acute disease or in convalescence. Anamnestic and epidemiologic data were collected. Stools and paired serums were obtained from 25 patients and 3 healthy family contacts (parents of sick children); conjunctival swabs were obtained from 8 patients. Samples of sewage were taken from the 2 localities. Adenovirus type 3 was isolated from the stools of 23 of 25 patients with "typical" symptoms and in

addition from the stools of 3 apparently healthy family contacts. The titer of fecal virus was high and some patients excreted the virus in their stools for at least 2 months. Virus was recovered from the sewage water of both communities involved in the epidemic. A serologic study performed after the epidemic on a larger group of persons confirmed the etiological correlation of the epidemic to adenovirus type 3 The symptoms were similar to those found by Bell and co-workers, with the exception that such gastrointestinal symptoms as nausea, vomiting, stomach-ache, and diarrhea were encountered in no less than about half of the patients. Some epidemiologic data are discussed and compared with those collected by Bell and coworkers.

Comparison of Ocular Reactions Using Penicillin and Bacitracin Ointments in Opthalmia Neonatorum Prophylaxis. A. M. Margileth. J. Pediat. 51:646-651 (Dec.) 1957 [St. Louis].

The use of penicillin opthalmic ointment was instituted in response to the high incidence (reported as 100% in some instances) of severe ocular reactions in newborn infant's eyes after the use of silver nitrate. The disadvantages of using penicillin in treatment of opthalmia neonatorum center on its ineffectiveness against most gram-negative organisms and the fact that severe ocular reactions may occur after a few instillations and that it is possible to sensitize the infant to penicillin at birth so that a systemic reaction may occur later in life. By contrast, bacitracin is bactericidal and is effective against many coccic (including the gonococcus) and some bacillary forms, is nontoxic when used topically, is of stable potency, and would rarely be used systemically later in life. Primary hypersensitivity reactions to bacitracin are rare, and the allergic manifestations are nil. Several authors have advocated that no prophylaxis be given at all or that simple irrigation of the eyes with saline solution or washing with Zephiran solution be done. This latter suggestion is the result of a decreased frequency of gonorrheal infections in the newborn period and the ability of antibiotics to control such infections quickly when they occur. It is attested to by the repeal by the Health Department of the city of New York of the requirement that prophylactic measures of any sort be taken at the time of birth for the prevention of opthalmia neonatorum and by the report of 18 instances of opthalmia neonatorum after silver nitrate prophylaxis.

There was no significant difference (bacitracin, 2.3%; penicillin, 4.2%) in the low number of ocular reactions or infections in either group of a total of 7,774 infants observed in a comparative study of the ocular reactions in the newborn period after the use of penicillin and bacitracin opthalmic ointments in the prophylaxis of opthalmia neonatorum. It is of note that all of the bacteria cultured in the bacitracin group were gram-negative and that no micrococci (staphylocci) were cultured. In view of the fact that most of the opthalmic ointment is washed out of the normal eye within 20 minutes, one might question the value of administering an antibiotic or silver nitrate in order to prevent an ocular infection, particularly when gonorrhea conjunctivitis can be treated so effectively with penicillin intramuscularly. Thus, careful observation of the newborn infant's eyes for several days after delivery for evidence of infection is considered the best prophylaxis; before definite conclusions are made and further evidence is revealed as to the necessity of using any prophylaxis at all, a safe, effective, and nonirritating bactericidal ointment should be used in the newborn infant's eyes. Bacitracin opthalmic ointment would appear to satisfy these criteria.

Observations on the Use of Novobiocin in Pediatric Pathology. S. Petrocini, D. Bullio and T. Battelli-Romizi. Minerva pediat. 9:893-901 (Sept. 8) 1957 (In Italian) [Turin, Italy].

Novobiocin was given to 33 hospitalized children with infections caused by Micrococcus pyogenes var. aureus and albus that have been resistant to other antibiotics. Rhinopharyngitis was present in 4 children, various types of pneumopathy in 11, skin infections in 3, suppurative adenitis in 8, cystitis in 2, gastroenteritis in 2, coxa femoral osteomyelitis in 1 and gluteal abscess in 2. A daily dose of 15 mg. per kilogram of body weight was given to the patients orally in 4 divided doses every 6 hours for a period of 6 to 8 days. Children with rhinopharyngitis became rapidly afebrile and no relapses occurred. A marked increase of antistaphylolysin blood level was observed. Children with pneumopathy became also rapidly afebrile, leukocyte counts returned to normal, and improvement of clinical and radiologic findings was seen. Patients with skin infections, suppurative adenitis, gluteal abscess, and coxa femoral osteomyelitis were also greatly improved by novobiocin. M. pyogenes var. aureus was present in the feces of 2 patients with gastroenteritis; within 4 days normal stools developed. The patient tolerated the therapy well. A patient who received novobiocin treatment longer than 10 days had a liquid stool for 2 days, which was corrected by discontinuing the therapy. Novobiocin medication was combined with parenteral administration of vitamins to anticipate signs of vitamin deficiency, which otherwise occurred 5-6 days after the onset of therapy. Allergic exanthema appeared in 1 child and was cured with antihistamines.

The opinion of the authors is that novobiocin is effective in infections caused by gram-positive bacilli, particularly by M. pyogenes var. aureus and

albus. No cross-resistance between novobiocin and other antibiotics was observed. Novobiocin therapy may be effective when prolonged therapies with other antibiotics have failed. Novobiocin exerts a synergistic effect with penicillin or with the tetracycline group of compounds or with other antibiotics.

INDUSTRIAL MEDICINE

Cancer of Larynx and Occupational Inhalation of Harmful Substances. H. Blümlein. München. med. Wchnschr. 99:1333-1335 (Sept. 13) 1957 (In German) [Munich, Germany].

Cancer of the larynx has become the most frequent cancer in the otorhinolaryngological field. Especially in men cancer of the larynx shows the same increasing incidence as does cancer of the lung. On the basis of anamnestic investigations the author concludes that the inhalation of tobacco tar during the smoking of cigarettes is an important factor in this increase. In addition, the prolonged inhalation of hot air seems to be a factor in the etiology of cancer of the larynx. Among 300 patients with cancer of the larynx observed at the University Clinic for Otorhinolaryngology in Erlangen, Germany, 53 patients had a history of occupational exposure to heat. These patients were stokers, locomotive engineers, tar and asphalt cookers, blacksmiths, bakers, glass blowers, and iron foundry workers. The author suggests that an occupational history be obtained from every patient with cancer of the respiratory tract and that the history should be without gap, covering the entire life of the patients. Some epidemiologic data are discussed and exogenous carcinogenic factors in human cancer usually extends over several decades.

THERAPEUTICS

Parenteral Iron Therapy: With Special Reference to a New Preparation for Intramuscular Injection. P. R. McCurdy, C. E. Rath and G. E. Meerkrebs. New England J. Med. 257:1147-1153 (Dec. 12) 1957 [Boston].

Sixty patients, 50 women and 7 men between 17 and 81 years of age and 3 male infants, with iron-deficiency anemia were treated with a preparation combining iron with a dextran of low molecular weight. The iron-dextran complex (Imferon) was injected intramuscularly into the upper outer quadrant of the buttock in doses ranging from 2 to 10 cc. (100 to 500 mg. of elemental iron). To minimize the risk of an untoward reaction, a test dose of 1 or 2 cc. was usually given and half an hour or more allowed to pass before more was injected. Usually, not more than 500 mg. was administered until a definite response was noted, as either a reticulocyte elevation or a change in hematocrit value. The total dose which was calculated according to a simple equation was then given rapidly (once or twice daily) to inpatients and more slowly (once weekly or less often) to outpatients.

The response to treatment of patients with uncomplicated iron-deficiency anemia was uniformly good. In some patients with disease complicated by infection, cancer, or liver disease the response was also good. When a good response was not obtained, a complicating disease was usually observed or the anemia was discovered to be due to some condition other than iron deficiency. Most patients reported local discomfort from the injection, similar in all respects to that experienced with any injection, although slightly more severe. It rarely lasted for more than 10 or 15 minutes. Pain radiating down the back of the leg was noted occasionally. Local discoloration of the skin at the injection sites owing to leakage along the needle tract was noted in 5 patients. One patient had an attack of giddiness and malaise during the hour after the injection, but the hematocrit level was 15 mm. at the time, and the symptoms may not have been related to the injection. Another patient had dyspnea, paresthesias, and epigastric pain for a short period 24 hours after injection of 500 mg. of iron. Although this could have represented the combined effect of anxiety and severe anemia, treatment was discontinued because of the possible reaction; this was the only case in which the drug was withdrawn because of side effects. The results suggest that the iron-dextran complex is both effective and relatively nontoxic and can be recommended when the parenteral route is indicated.

The Place of Métacortandracine (Prednisone) in the Treatment of Icterogenic Hepatitis: Comparison with the Classic Treatment. J.-A. Colson, H. Garnung, R. Hugonot and others. Presse méd. 65: 1903-1904 (Nov. 23) 1957 (In French) [Paris].

In the course of an epidemic of icterogenic hepatitis, 100 patients were given the classic treatment with 2 Gm. of methionine combined with vegetable extracts of artichoke type (Chophytol) by intravenous route and administration of Bourget's solution, consisting of sodium sulfate, sodium bicarbonate, and sodium phosphate, for 2 weeks. Métacortandracine, a French preparation of prednisone, was given to 100 other patients for 10 days with a total dose of 220 mg. Comparison of the results obtained in these 2 groups of patients revealed that prednisone therapy had several advantages over the classic treatment. The general condition of the patient improved more rapidly in that adynamia and apathy disappeared within 48 hours, making it possible for the patient to get out of bed and to regain his appetite. The course of

the disease was shortened. The cutaneous pigmentation decreased rapidly. Satisfactory diuresis was restored rapidly after the episode of polyuria. Cholesteremia and bilirubinemia were restored more rapidly to normal, but the effect of prednisone therapy on the serologic tests was not more consistent than that of the classic treatment. Recurrences were less frequent after prednisone therapy than after the classic treatment and responded well to repeated prednisone therapy. Two of 3 patients with icterus of more than 3 weeks duration showed a less favorable response to the prednisone therapy. Undesirable side-effects of prednisone therapy were not observed. A neurological complication occurred in 1 patient. Although prednisone therapy does not provide complete protection against relapses and complications, it should be preferred to the classic treatment.

PATHOLOGY

Studies in Achalasia of the Cardia. J. R. Trounce, D. C. Deuchar, R. Kauntze and G. A. Thomas. Quart. J. Med. 26:433-443 (Oct.) 1957 [Oxford, England].

Longitudinal muscle strips from the lower end of the esophagus of a group of patients with achalasia of the cardia were studied and compared with muscle from a similar region in patients without achalasia. In vitro experiments showed that strips from both groups of patients behave pharmacologically as smooth muscle, that there is present a mechanism involving cholinesterase, and that in both groups the majority of specimens contain active ganglion cells. The cholinesterase of muscle samples from both groups showed similar activity. The histological picture was variable, but approximately normal numbers of ganglion cells were found in 2 out of 6 samples from patients with achalasia. Thus, in patients with moderately severe and advanced achalasia of the cardia, it is still possible to elicit evidence of active ganglion cells in the narrowed segment at the lower end of the esophagus in the majority of cases. Such findings are opposed to the view that the failure of the cardia to relax is necessarily due to degeneration of ganglion cells in that region.

The demonstration of active ganglion cells in the lower segment of the esophagus in all but 2 of the patients with achalasia was surprising in view of the number of reports of complete or almost complete absence of these cells from this region. It might be suggested that the disease is progressive and that in time the ganglion-cells would have disappeared in these patients. Such a supposition seems unlikely, for in a patient with advanced achalasia of at least 25 years an approximately normal number of cells was found histologically in a specimen which had previously shown pharmacological activity. It seems probable that ganglion-cell degeneration is confined in certain cases to the dilated portion of the esophagus above the obstruction and that previous studies of the histology of this condition have missed this small lower section, which becomes inconspicuous after death. The factors governing the relaxation of the lower end of the esophagus are not fully understood, but it is not unreasonable to suppose that, if the function of the main body of the esophagus were disordered, the lower end might not receive the normal stimulus to relax. There is considerable evidence that the function of the main body of the esophagus is abnormal in achalasia and that normal peristaltic waves do not appear. Many histological studies have suggested that in this region there is a diminution or absence of ganglion cells. It is therefore possible that the continued tonus of the lower segment is due to a disturbance in function of the main part of the esophagus rather than to any abnormality in the region of the cardia itself.

Primary Acute Pulmonary Histoplasmosis. A. González Ochoa. Gac. méd. México 87:733-743 (Oct.) 1957 (In Spanish) [México, D. F.].

The discovery of primary acute pulmonary histoplasmosis in the United States of America in 1950 made it possible for Mexico to organize etiological reconstruction of the various epidemics of the disease which have occurred in the country between 1948 and 1950. It also enabled epidemiologists to carry out more complete studies of new epidemics. The disease was known in Mexico for a long time under the names of "fever of the abandoned mines" or "fever of the caves." The disease appears in epidemics only among people who have been in the following circumstances: (1) staying inside of an abandoned mine or cave exposed to air highly contaminated with bats' dung, or (2) handling bats' dung. The disease appears within 6 to 9 days after exposure. The first respiratory symptoms manifest themselves as fever, dyspnea, cough, and cyanosis. The chest roentgenograms are typical, showing a particular type of pneumonitis which simulates miliary tuberculous infiltration. The disease runs a severe course for the first 2 or 4 weeks. The skin reaction to histoplasmin becomes positive at any time after the end of the third week of the illness. Death occurs as a rule within the first 2 weeks of the disease, with acute symptoms of alveolar capillary blockage. Convalescence takes place in 3 to 6 months. The pulmonary infiltration undergoes calcification in 33% of the cases. Either disappearance or calcification of pulmonary lesions occurs late after recovery.

Eight epidemics have been observed in Mexico between 1948 and 1956. The patients were persons who gathered bats' dung to be sold as a fertilizer,

tourists, students, or geologists uncovering and sampling mineral veins. The epidemics of primary pulmonary histoplasmosis in Mexico are severe. The disease is not restricted to 1 or more geographic zones but is found in the mine regions of the states Coahuila, Durango, Tamaulipas, San Luis Potosi, Queretaro, Nayarit, and Yucatan, which are distant from one another.

Immunoelectrophoretic Study of Gamma Globulins: Identification of Several Antigenic Determinants with the Aid of Bence-Jones Proteins and Serums Obtained from Patients with Myeloma. J.-J. Scheidegger and C. Buzzi. Rev. franç. étud. clin et biol. 2:895-906 (Nov.) 1957 (In French) [Paris].

The authors performed immunoelectrophoretic studies on serums obtained from 7 patients with multiple myeloma (2 of which were of paper electrophoretic beta type and 5 of paper electrophoretic gamma type), on Bence-Jones proteins isolated from the urine of 2 patients, and on gamma globulins obtained from normal human serums. Results showed that normal gamma globulins have at least 4 groupings determining antigenic properties. Bence-Jones proteins have one of these groupings and can be considered as gamma globulin fragments. Serum myeloma proteins are abnormal, incomplete gamma globulins, with 1 or more groupings missing. The use of a preparation of gamma globulins tagged with radioactive iodine (I^{131}) for the immunoelectrophoretic study made it possible to separate normal and pathological gamma globulins.

It has further been shown that each antigenic determining grouping is specific for a single antibody, with the result that the term "anti-gamma globulin" covers a mixture of at least 4 different antibodies. Immunoelectrophoresis has shown the existence of these antibodies, as well as a difference in their electrophoretic mobility. Immune serums are not identical and may contain these antibodies in variable proportions. Certain groupings may be more strongly antigenic than others.

RADIOLOGY

Visibility of the Appendiceal Stump on the Roentgenogram of the Colon. D. Limburg. Nederl. tijdschr. geneesk. 101:1754-1757 (Sept. 21) 1957 (In Dutch) [Amsterdam].

The author describes the roentgenogram of the cecum after the introduction of contrast medium in some patients who had undergone appendicectomy. He found that in such patients the roentgenogram may show a round gap in the barium filling of the cecum, due to a large, invaginated appendiceal stump. Roentgenologically this defect in filling cannot be differentiated from a number of other filling defects and thus may be taken for an indication for a laparotomy. Occasionally fecoliths may cause such a filling defect. A roentgenogram of the cecum was made in a small number of patients shortly after an appendectomy had been performed; a round filling defect was observed in 1 of these patients. The author recommends that, during appendectomy, the appendiceal stump should be made as small as possible.

PHYSIOLOGY

An Abnormality of Nonesterified Fatty Acid Metabolism in Diabetes Mellitus. E. L. Bierman, V. P. Dole and T. N. Roberts. Diabetes 6:474-479 (Nov.-Dec.) 1957 [New York].

In normal subjects nonesterified fatty acid (NEFA) concentration falls sharply after an injection of insulin, paralleling the fall of blood glucose levels. The injection of glucose or glucagon will cause the NEFA and glucose levels to vary in opposite directions (blood glucose rises while NEFA falls). The common denominator in the fall of NEFA concentration in these 2 situations is an increased utilization of glucose promoted by insulin or an extra input of glucose in the presence of adequate endogenous insulin. Diabetic patients show an abnormally prolonged elevation of blood sugar level after a glucose load and a reduced capacity to burn carbohydrate or synthesize fat. The present study indicates a commensurate increased NEFA concentration abnormality in such patients.

The NEFA level of 40 fasting, nondiabetic, nonobese subjects averaged 572 mEq per liter, the level of 7 diabetics without ketosis averaged 849 mEq. per liter, and that of 10 diabetics with ketonuria averaged 1,311 mEq per liter. Obese nondiabetic patients resembled the controlled diabetic patients in elevation of NEFA levels. Glucose tolerance tests or injection of glucagon in diabetic patients resulted in an abnormally prolonged but comparatively weak fall of NEFA level. The usual sharp fall in NEFA concentration and return to control values was delayed and diminished in amplitude, corresponding to the delayed return of blood sugar concentration. Injection of insulin into patients with acidosis caused a dramatic fall in NEFA concentration, paralleling the fall in the blood sugar level and preceding by several hours the elimination of ketone bodies. The wide range of data even within divergent groups demonstrates the lability of this fraction, emphasizes the need for standard conditions and repeated measurements, and suggests that measurement of NEFA level may lead to a more complete and comprehensive clinical evaluation of the metabolic defects in diabetes.

BOOK REVIEWS

The Diagnosis and Treatment of Infections. By D. Geraint James, M.A., M.D., M.R.C.P., Clinical Assistant, Middlesex Hospital, London. Cloth. $6. Pp. 234, with 1 illustration. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

This is the sort of book on infectious diseases that the busy practitioner has been waiting for. It should also be welcomed by students, interns, and residents as an easily usable reference work or for quick review. It is brief, up-to-date, well organized, written in an easily readable style, and has some excellent and informative tables. Little of importance has been omitted. The material is presented in three parts. Part 1 describes the generally available chemotherapeutic agents, their range of activity, indications for their use, the forms in which they are available, and the recommended dosage. The fate of the agents in the body and the complications of their clinical use are discussed in separate chapters. Part 2 is presented from the point of view of the common pathogenic microorganisms, with descriptions of the infections they may produce, some diagnostic features, and the best methods for treating those infections. Part 3 covers the infections of systems and organs and their diagnosis and treatment. This part ends with separate chapters dealing with pyrexia of unknown origin and the use of corticosteroids in the management of infections.

Cancer. Volume 1, Part 1: Research into Causation. Edited by Ronald W. Raven, O.B.E., T.D., F.R.C.S., Joint Lecturer in Surgery, Westminster Medical School, University of London, London. [To be in six volumes.] Cloth. $18. Pp. 558, with 94 illustrations. Butterworth & Co. (Publishers) Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada, 1957.

This is the first volume of an ambitious six-volume work. The prospectus indicates that practically all aspects of cancer will be considered in the complete publication. The first volume is on research into causation. The British and American contributors are active research workers in cancer, and their view-point is mature, yet in the main the presentations espouse no particular theory but marshal the facts and the findings in a comprehensive, scholarly, yet critical fashion. Since any review on cancer research can be no more than a progress report, many of the authors attempt to suggest profitable developments of future research.

The first chapter, on the historical aspects of cancer, by W. R. Bett, is the weakest. It is not only sketchy but partially erroneous regarding several important events. Although cancer, as all incompleted research, chronicles errors, illusions, and disappointments, its occasional triumphs should be attributed correctly and claims to priority should be documented at least by citing the primary sources. Bett states that Le Dran in 1757 upset Galen's theories about cancer. As a matter of fact, the local tissue origin of cancer and the rejection of the humoral hypothesis are clearly presented in Gendron's book published in 1700 (Mustacchi and Shimkin, *Cancer* 9:645 [July-Aug.] 1956.) Joseph Leidy is stated to have "reported the first experimental transplantation of a malignant tumor" in 1851. Leidy (*Am. J. M. Sc.* 22:555, 1851) implanted human mammary cancer into frogs and noted the maintenance of a vascularized mass for some days. Careful reading of his short communication allows no conclusion, even in retrospect, of successful transplantation of a tumor. This advance, usually credited to Hanau in 1889, is better attributed to Novinsky, in 1876 (Shimkin, *Cancer* 8:653 [July-Aug.] 1955). Experimental cancer is recorded as having been produced by Bayon in 1912. Bayon (*Lancet* 2:1579, 1912) injected gasworks tar into ears of rabbits, and sacrificed them four weeks later. He observed epithelial hyperplasia and probably would have achieved malignant neoplasia had he waited, but the honor of inducing carcinoma with tar remains firmly with Yamagiwa and Ichikawa.

Sir Ernest Kenneway contributes two short chapters on the incubation period of cancer in man and on the carcinogenic effect of cholesterol. The latter should serve in the necessary revitalization of chemical studies in cancer, based on the old hypothesis that cholesterol is a parent molecule of endogenous carcinogens. P. R. Peacock, J. N. Davidson, and A. C. Griffin deal with the biochemical aspects of carcinogenesis in the next three chapters. It is interesting that in comparison with research of 20 years ago, when carcinogenesis was treated usually from the standpoint of chemicals that induce neoplasia, the present approach is concerned primarily with the tissue, cellular, or subcellular reactions. In fact, no specific chapter on chemical carcinogens per se is found in the book. The subject of hormones and cancer is reviewed by M. B. Shimkin and the tumor viruses by L. Dmochowski. Both are carefully thorough jobs, with conservative

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

generalizations and open conclusions. A. Tannenbaum and H. Silverstone summarize the investigations on the role of diet in carcinogenesis.

P. C. Koller's chapter on the genetic component of cancer is outstanding in its clarity and completeness, covering human as well as animal data. Genetics has contributed much to cancer research in the past. This review promises continued productiveness, particularly through collaborative endeavors of geneticists and biochemists on the one end of the scale and of geneticists, statisticians, and clinicians on the other. The chapter on environmental carcinogenesis by W. C. Hueper indicates clearly the innumerable carcinogenic stimuli faced by man and the research challenge this poses, but it attempts to present too much data at the expense of evaluation. This is particularly true in the long discussion of the "cigarette theory of cancer." A. Glucksmann, L. F. Lamberton, and W. V. Mayneord in the last chapter present a thoughtful discussion of the carcinogenic effects of radiation.

The prospectus shows that a number of chapters on the cause of cancer will appear in future volumes and will probably fill some of the gaps in the first volume, but even as it stands this first volume gives impressive evidence of how far cancer research has progresssed since Jacob Wolff's monumental collation in the four-volume "Die Lehre von der Krebskrankheit" of 1907-1928. "Cancer" will long remain one of the standard reference books on the subject. It is well printed and generously illustrated, the format and the binding are pleasing, and the references are fully given. Every investigator and student of cancer should have access to it.

Mental Deficiency. By L. T. Hilliard, M.A., M.B., D.P.M., Consultant Psychiatrist and Physician Superintendent, Fountain Hospital, London, and Brian H. Kirman, M.D., D.P.M., Consultant Psychiatrist, Fountain Hospital. With assistance of four contributors: L. Crome, M.C., M.R.C.P., Neil O'Connor, M.A., Ph.D., J. Tizard, M.A., B. Litt, Ph.D., and Elizabeth Williams, M.A.O.T. Cloth. $10. Pp. 517, with 90 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England, 1957.

Although this book is primarily concerned with the mental deficiencies resulting from abnormal development of the brain and therefore generally having unknown causes, it also includes a review of those diseases of definitely defective development, such as metabolic conditions, vascular conditions, and specific developmental defects of the brain. In addition to this, it takes into account metabolic, traumatic, and infectious insults occurring prenatally, natally, and postnatally. It presents a comprehensive review of the problem from the legal, administrative, and social angles and deals with cause, pathology, treatment, and training. Although the legal and administrative aspects are described as they exist in England, the conclusions are generally applicable. The book presents little that is new, but it does serve the useful purpose of orienting those people in the medical and allied professions who may encounter the problems of mental deficiency as part of their professional work. The most revealing aspect of this work is the proof that persons with mental deficiency, even of rather low grade, under proper training and supervision can accomplish a rather remarkable amount in the way of self care, productive work, and integration into some phase of the social order. Developing these persons from unhappy, useless, institutional inmates to individuals of useful though limited productivity has been an outstanding accomplishment of those working in this field.

Clinical Electrocardiography: The Spatial Vector Approach. By Robert P. Grant, M.D. Cloth. $7.50. Pp. 225, with 95 illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1957.

This book presents a novel approach to the diagnostic use of the conventional 12-lead electrocardiogram. The author has for many years championed the use of vector graphs derived from standard electrocardiograms as a method of teaching electrocardiography. In 1951, he and Estes published a book entitled "Spatial Vector Electrocardiography." Largely because the plotting methods originally described were cumbersome and time-consuming, his methods have not had wide acceptance. The technique has now been simplified so that points from which the loops can be drawn are easily plotted after inspection of the electrocardiogram. Although it is conceded that this method is rather crude, the author points out that the many difficulties and shortcomings of cathode-tube vector-cardiography are much greater, limit its usefulness to research workers, and preclude its use in clinical electrocardiography. The method described in this book is particularly useful in teaching. It is probably the best method available to clarify the concept of electrical position using standard 12-lead electrocardiograms. The chapter on myocardial infarction is excellent, but that on arrhythmias and on congenital heart disease is too short. The text is clear and easy to follow. It is supplemented by numerous diagrams and line drawings. A few references are given at the end of the book, and there is an index. This book is recommended not only for the student of electrocardiography but also for the cardiologist who would like a fresh approach to the subject of electrocardiography.

QUESTIONS AND ANSWERS

CANCER OF THE CERVIX

To the Editor:—*A 60-year-old woman had a biopsy for cancer of the cervix. The diagnosis was carcinoma in situ of cervix. A week later a conization was performed to certify the diagnosis. The result was a diagnosis of carcinoma of the cervix, grade III, stage one. The patient does not want to undergo surgery or radiation and claims that she might have been cured by the conization. Can a cancer of the cervix be cured by conization without surgery or radiation following?*

Walter M. Lehmann, M.D., Carmel, Calif.

Answer.—The diagnosis of cancer in situ of the cervix demands that the attending physician establish this fact without any chance of error. Therefore, conization of the cervix and sample sectioning of the many blocks are accepted procedures. This case illustrates the need for such thorough study of the squamocolumnar junction of the cervix. The treatment of invasive carcinoma is x-ray and radium or radical hysterectomy and lymph node dissection. No one would take the risk of assuming that simple conization has removed all of the cancer bearing area. This patient should be told that she has invasive cancer, that there are only two accepted treatments, and that if she refuses to submit to such therapy, she is responsible for whatever might occur due to spread and invasion of the primary lesion.

TREATMENT OF DERMATITIS HERPETIFORMIS

To the Editor:—*Is there any effective or promising treatment, other than sulfapyridine, for dermatitis herpetiformis? Is there any reason to believe that iproniazid would be helpful?*

M. E. K. Johnson, M.D., Kalispell, Mont.

Answer.—Many therapeutic agents, in addition to sulfapyridine, have proven to be effective in controlling eruptions of dermatitis herpetiformis. In some instances, other sulfonamides have given results equal to those obtained with sulfapyridine and with fewer toxic manifestations. Some authorities tend to disagree on the effectiveness of other sulfa drugs, but personal experience with sulfadiazine, triple sulfas, etc. has been gratifying. Among the more effective agents is potassium arsenite (Fowler's) solution. However, this pentavalent inorganic arsenical is not employed at this time in cases of chronic dermatoses, including keratoses and squamous-cell epitheliomas, because of late toxicity. The latter, when on the palms and soles, may metastasize to regional lymph nodes, making the use of this agent inadvisable. Sulfoxone sodium, 0.3 to 0.9 grams per day, and other sulfones have proven efficacious in some instances of this disease. Nicotinamide, in large doses, will control some cases. Probably corticosteroids are as effective as any agent in this disease, and the toxicity is no greater than with sulfones, sulfonamides, etc. A long acting corticotropin could be administered intramuscularly in doses of 40 units from twice weekly to daily. If oral medication is preferred, cortisone could be used in a dose of 300 mg. the first day, 200 mg. the second day, and then 100 mg. daily in divided doses. Further modifications of dosage would be indicated by clinical progression and results. Corticosteroids could be substituted for cortisone in equivalent dosage if desired. Many of the aforementioned agents contain a modified nicotinic acid-type radical. A therapeutic trial of iproniazid in dermatitis herpetiformis would be a reasonable procedure. However, lack of personal experience by this consultant with this agent makes an answer regarding its clinical efficacy impossible at this time. Incidentally, it might be mentioned that dermatitis herpetiformis tends to "burn itself out" after 10 to 20 years, so spontaneous cure is to be expected. With this in mind, it is wise to consider seriously the potential toxicity of any agent introduced for the treatment of this condition.

THERAPY WITH MINERAL PREPARATIONS

To the Editor:—*More and more minerals are being added to vitamin-mineral preparations. 1. How necessary are these minerals? 2. Just what is their function? 3. How many minerals are actually present in the various tissues and organs of the human body?*

H. Curtis Wood Jr., M.D., Philadelphia, Pa.

Answer.—The A. M. A. Council on Foods and Nutrition has just finished preparation of a statement on vitamin preparation as dietary supplements and as therapeutic agents. This statement, soon to be published in The Journal and available from the Council on Foods and Nutrition, is intended as a guide to the physicians using multivitamins and states that there is little or no justification for the inclusion of minerals in vitamin preparations. Calcium and iron are exceptions in preparations in-

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

tended for use in gestation and lactation. The well-balanced diet can be counted on to supply all mineral elements needed for proper nutrition.

The mere presence in the body of an element does not constitute sufficient evidence that it is required. The body is exposed to so many elements from the food we eat, the water we drink, and the air we breathe that it seems likely one could probably find a trace of all the elements in the periodic table. Until we know more about the detoxification of nonrequired elements and inert storage of them, it might be best to assume, for example, that most of the elements listed as having been found in the human body are there by happenstance. Except for special situations, there is no rationale for extradietary ingestion of mineral preparations as compounded with multivitamins.

DIAMETER OF RETINAL BLOOD VESSELS

To the Editor:—*What are the average calibers of the retinal artery and vein at the disk margin?*

M.D., Mexico.

Answer.—Hertel (*Arch. f. Ophth.* **52**:191-222, 1901) found the average diameter of the central retinal artery during life to be 212.1 μ in the 25-to-30-year range and 210.2 μ at about 60 years. The average diameter of the central vein was 228.9 μ in the 25-to-30-year group and 234 μ at about 60 years.

EXCESSIVE RELAXATION OF PELVIC JOINTS DURING PREGNANCY

To the Editor:—*About the middle of the fifth month of pregnancy, a 29-year-old woman suddenly developed a sharp, paralyzing pain in her right hip "like I had pinched a nerve." She continued to have such spells, which became more frequent and more severe until after the birth of her child. Shortly after delivery (under saddle-block anesthesia) she was perfectly normal and free of pain. In her second pregnancy the pains started the latter part of the second month. They were more frequent and gradually more severe, always in her right hip and leg, and occurred mostly when she was in a prone or a stooping position. On one occasion she was taking a bath and had to call her husband to lift her out of the tub. After her second labor she improved immediately and is now perfectly well. Perhaps she may have a natural excess of a relaxing hormone, since she has short easy labors. Could such symptoms be caused by a relaxation in some of the joints during pregnancy?*

Frank W. McCorkle, M.D., Gadsden, Ala.

Answer.—The supposition that the pains in the case cited were due to excessive relaxation of one or more pelvic joints resulting from an overabundance of a relaxing hormone elaborated during gestation may be correct. If this is so, the following is pertinent. Greenhill (Obstetrics, ed. 11, Philadelphia, W. B. Saunders Company, 1955, p. 538) says: "The advent of x-rays changed many old and erroneous ideas concerning the pelvis. It is now known that: (1) pregnancy causes relaxation of the pubic joint as evidenced by a separation of the pubic bones; (2) the amount of separation varies, being pathologic in some cases; (3) the relaxation of the joint begins during the first half of pregnancy, reaches a maximum at the seventh month and does not increase during labor; (4) the amount of relaxation diminishes after labor and returns to the nonpregnant state within six months; and (5) a similar change probably occurs in the sacroiliac joints.

"According to Young, the disabilities arising from excessive relaxation of the pelvic joints fall under two headings: (1) those dependent on excessive mobility at both the sacroiliac and the pubic joints and (2) those dependent on an excessive mobility at the sacroiliac joints alone. He believes that clinical symptoms arise more often from sacroiliac relaxation than from pelvic loosening. In place of the expression 'excessive relaxation of the pelvic joints during pregnancy' Young suggests 'pelvic arthropathy of pregnancy' with its variants 'sacroiliac arthropathy' and 'pubosacroiliac arthropathy.' In a series of 4,512 pregnant women these arthropathies occurred thirty-four times, an incidence of 0.75 per cent. . . .

"The chief symptoms of undue pelvic mobility are pain and tenderness in the pubic and sacroiliac joints which first appear about the sixth or seventh month of pregnancy. In the beginning the patient experiences pain only on walking and during exertion. The pain may appear suddenly. The pain may be so severe that walking or even standing is impossible and in these patients there is excruciating pain when they turn in bed or are placed on a bedpan. The gait is usually affected, when mild there is a limp on one side and when severe there is a side-to-side waddle.

"One of the most characteristic signs is tenderness on pressure over the pubic joint and the affected sacroiliac joint. . . .

"In mild cases relief can be obtained by the wearing of a properly fitting girdle and some restriction of activities. The girdle should be worn for a few months after delivery. For severe cases complete rest in bed is necessary. After seven to ten days the patient may get up but she must wear a strong support. In a few instances not only must patients be placed in bed but they must be kept in slings similar to those used for fractured pelves. This treatment may have to be continued throughout the remainder of the pregnancy and for a few weeks after delivery.

"The management of patients during labor is important, particularly if inhalation anesthesia is used. Under such circumstances the patients cannot protect themselves by voluntary muscular control. Therefore movements of the pelvis or limbs may

cause damage to the softened or vulnerable joints. The lithotomy position is particularly harmful (Young)."

GEOGRAPHIC TONGUE

To the Editor:—*What is the cause, prognosis, and newest treatment of geographic tongue?*

Edmund C. Wallner, M.D., Troy, N. Y.

Answer.—This is a benign type of coating of the tongue in which the deposit or furring arranges itself in such a manner as to simulate a geographical map. It is known also as erythema migrans, glossitis areata exfoliativa, or "wandering rash." It is an asymptomatic superficial migratory deposit on the tongue, noninflammatory in nature, and slowly changes from day to day. Usually it is confined to the dorsum and sides of the tongue; the lesion begins as a central deposit and extends itself distally by concentric rings at times; the individual patches coalesce, giving rise to polycyclic figures which represent the geographic tongue. The condition is fairly common and has no clinical significance. It tends to be persistent and is prone to relapses. Its etiology is unknown; treatment apart from prophylactic oral hygiene is not necessary.

AORTIC ANEURYSM

To the Editor:—*A 31-year-old man has had a diagnosis of aneurysm of the arch of the aorta since 1953. This aneurysm has been demonstrated by fluoroscopic studies and by angiocardiography, which, however, was not entirely satisfactory. There is some calcification in the aneurysm. There has been no change in the size of the aneurysm on routine x-rays repeated every six months. The patient was seen by several consultants who did not recommend any surgical intervention since there has been no change in the size of the aneurysm. The patient works every day and complains only of dyspnea on unusual exertion. His physical examination is essentially negative. There is no cardiac enlargement. There is regular sinus rhythm. Both radial pulses are equal and synchronous. Blood pressure in the right arm is 130/80 mm. Hg and in the left arm is 124/80. What treatment is advised in this case, and what is the prognosis?*

M.D., Ohio.

Answer.—If, because of the circumstances in this particular case, resection of the aneurysm with insertion of an arterial homograph is not deemed advisable, the patient should be advised to avoid unusual exertion such as heavy lifting and straining. Whereas spontaneous rupture is very common, the increased arterial pressure occasioned by muscular effort would predispose to enlargement and possible rupture of the aneurysm. There is no information given as to the size or shape of the aneurysm, whether saccular or dissecting, etc. One would conclude that it is fairly small in view of the absence of pressure symptoms, and this fact together with its apparent stability over a five-year period might well imply a favorable prognosis; however, the age of the patient and the location of the aneurysm would speak for a dissecting aneurysm rather than an arteriosclerotic or syphilitic one and a further dissection could conceivably occur at any time.

NEVUS FLAMMEUS

To the Editor:—*For 10 years a patient has suffered from chronic eczema located solely on a birthmark. It is a nevus flammeus located on the right mental, right mandibular, and right cervical regions, extending up into the scalp. It has received a great deal of treatment but does not respond. The patient's urine contained 4% lead on one occasion. Other specimens have been normal. She works as a "solderer" and was quite free of cutaneous disease before being so employed. A physical examination was normal in all respects. Cortisone ointments help but do not cure the condition. Please give suggestions, particularly as to treatment and etiology.*

M.D., Massachusetts.

Answer.—The causes of an eczematoid eruption are nearly limitless. Lead, per se, is not dermatogenic. Soldering is not apt to cause such an eruption, although ammonium chloride is a recognized cause of dermatitis. A nevus flammeus is seldom involved selectively in such a condition. The possibility of a fixed-drug eruption occurring in an area of lowered resistance must be considered. This could be due to a laxative, tonic, or analgesic, etc. Excision of the nevus followed by grafting might eliminate the dermatitis or might prove to be ineffective in this case. It would necessitate a great gamble in money and time with no assurance of results.

SUDDEN BLOOD PRESSURE FALL WITH HYPOTENSIVE DRUGS

To the Editor:—*On a moderate dosage of a ganglionic-blocking drug, some patients manifest sudden and profound blood pressure drops to systolic levels as low as 70 or 60 mm. Hg. Have these blood pressure changes (often associated with extreme pallor and dizziness) ever resulted in cerebrovascular or cardiac catastrophe?*

Alfred Soffer, M.D., Rochester, N. Y.

Answer.—The sudden and marked drops in blood pressure that can occur with ganglionic-blocking drugs can and do result in cerebrovascular and cardiac catastrophes. The decrease in blood flow during syncopal or near syncopal attacks brought on by these drugs not infrequently produces anginal pain when none has been present before. Death from multiple myocardial infarctions has been reported.

Cerebral thrombosis has been related to the drops in blood pressure. A standard story (true or not) is of the patient who developed hypotension in a telephone booth and died because he was prevented from falling to a horizontal position. This consultant has had patients with anginal pain as a result of hypotension but has had no major mishaps and therefore maintains a respect for these drugs. It is believed that they are not indicated in most patients with essential hypertension in whom they are being used.

ALLERGY TO MUSHROOMS

To the Editor:—*A 53-year-old man has, for many years, had violent gastrointestinal upsets with nausea and vomiting occurring regularly about three to four hours after the ingestion of a meal containing fresh mushrooms prepared in any form. Relief follows the vomiting of the complete meal. The reaction does not occur when dried mushrooms are used. Please advise whether parenteral or oral desensitization with mushroom extracts may be expected to give any degree of tolerance. If feasible, this procedure is desirable, since attacks frequently occur from meals containing mushrooms which have been disguised in sauces, gravies, or other accessories to the meal.*

M.D., New Jersey.

Answer.—Parenteral or oral desensitization with mushroom extract seems completely unnecessary. That particular food is quite easily detected, both as mushrooms and in vehicles which might contain mushroom. Avoidance is the main treatment. It might be well to prove the allergy to mushroom by doing a scratch test with mushroom extract. Incidentally, mushrooms, yeasts, and various fungi are closely related. Therefore, while the skin tests for mushrooms are being done, skin tests should also be done for the yeasts and fungi.

THE UNFORGIVABLE SIN

To the Editor:—*Women suffering from melancholia agitata often state that they are guilty of, or have committed, the original sin. What do they mean by this statement?* *M.D., West Virginia.*

Answer.—There is a confusion in name here. They mean the unforgivable sin, not the original sin. Original sin in theology refers to partaking of humanity and inherited responsibility for the sin of Adam. The unforgivable sin refers to Jesus' statement that all sins would be forgiven, except the sin against the Holy Ghost. The Holy Ghost keeps you sensitive to your obligations, gives you qualms when you do wrong, etc. Hence, if you finally stifle it by ignoring its promptings, you can become amoral, beyond reach, and lost. This is what George Washington meant by the copybook maxim: "Labor to keep alive in thy breast the spark of celestial fire known as conscience." Any one who is worried has obviously not committed the unforgivable sin. However, such considerations usually do not help neurotic or psychotic people whose basic condition is loneliness and abandonment and which they try to explain by reference to imaginary guilty acts.

PERSISTENT ALBUMINURIA WITH NEPHROSIS

To the Editor:—*A 7-year-old girl with nephrosis over a period of nine weeks has a slight residual edema, a 4+ persistent albuminuria, and a persistently elevated sedimentation rate. Would cortisone therapy be indicated? If so, at what time should it be given, in what dosage, and for what length of time?*

Robert E. Sandlin, M.D., Antioch, Calif.

Answer.—This child has had a relatively short course and had done fairly well. The albuminuria as well as the elevated sedimentation rate may persist for some time. A diet low in salt and high in protein should be prescribed and strictly followed. The aim in therapy should be to prevent infections (respiratory) and to allow the child to continue to recover. Some form of long-acting penicillin (125 mg. three times daily) should be given orally for at least six months to prevent infection with streptococci and pneumococci.

RADIUM IN TREATMENT OF FIBROID TUMORS

To the Editor:—*Please give indications for, and contraindications to, use of radium in treatment of fibroid tumor of uterus.* *M.D., Kentucky.*

Answer.—There is only one indication for the use of radium in the treatment of a fibroid tumor of the uterus and that is abnormal or excessive uterine bleeding. The contraindications for its use are far more important and limit its use to the rare patient. These contraindications, as usually stated, are a patient who is at the child-bearing age, tumor and uterus the size of a three or four month fetus, a tumor that is pedunculated, associated pelvic pathology, or pain and tenderness in the area. Naturally a combination of these findings would tend to make the contraindication even more valid.

INFERTILITY OF PROSTITUTES

To the Editor:—*Why do prostitutes never become pregnant, although no contraceptives are used?*

M.D., Canada.

Answer.—It is true that prostitutes rarely become pregnant, although contraceptives are rarely used. This can be explained by the occurrence of pelvic inflammatory disease following gonorrhea or postabortion. Mechanical factors due to peritubal and periovarian adhesions are usually stated as explanations, although emotional factors as well as the possible immunological effects of multiple sources of semen should be given some consideration.

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A. M. A. MEMBERSHIP

To the Editor:—*Is an active member of a state medical society automatically a member of the A. M. A.? Is the A. M. A. continuing to assess its members $25 as was done in 1949?*

M.D., Idaho.

Answer.—Several changes have taken place in the membership and fellowship structure of the A. M. A. from 1949 through 1958. From 1913 to 1949 all physicians who were active members of their state society were non-dues-paying members of the A. M. A. Of the 144,211 members of the A. M. A. in June, 1949, a total of 77,723 were listed as Fellows. Fellowship in the A. M. A. was dependent upon membership in the state medical society. Fellows paid dues ($12) directly to the A. M. A. and received The Journal or, if they so elected, one of the special journals. In 1949 the House of Delegates of the A. M. A. assessed all members $25, but this assessment was not compulsory. This was the only assessment made. Fellows still paid dues of $12 and received The Journal. In 1950 there was no assessment. Membership dues of $25 a year, however, were established. If these dues were not paid the member was dropped. Before he could be reinstated it was necessary for him to pay the delinquent year's dues. The 1950 membership dues did not include a subscription to The Journal. A member who was also a Fellow was asked to pay fellowship dues ($12) in addition to membership dues and received The Journal; non-Fellows subscribed to it separately. In 1951 the membership dues in the A. M. A. were $25 and for the first time included a subscription to The Journal. Fellowship dues were reduced to $5, in addition to membership dues, and no longer included a subscription to The Journal. From 1952 to 1958 membership dues have been $25. Fellowship in the A. M. A. was abolished in June, 1952. Dues-paying members of the A. M. A. receive their choice of one of the 10 scientific publications of the A. M. A. as a benefit of membership. Membership dues in the A. M. A. have never included fellowship dues. Membership dues are payable only through the county and state medical societies and not directly to A. M. A.

JOINING THE A. M. A.

To the Editor:—*What is the proper procedure for a physician who has recently completed internship and started the practice of medicine and who would like to join the A. M. A.?*

M.D., Illinois.

Answer.—Membership in the A. M. A. is dependent upon membership in the physician's county and state or territorial medical society. A member in good standing of a constituent association of the A. M. A. is eligible for either active or associate membership in the A. M. A. However, request for such membership should be made through the secretary of the component county and constituent state society where a physician conducts his professional activities.

ALTERATION OF TOOTH COLOR

To the Editor:—*In* The Journal, *Jan. 4, 1958, page 111, is a question and answer relative to alteration of tooth color. The answer is correct except for the sodium fluoride treatment recommended. Applied to tooth areas of this type, sodium fluoride is almost certain to turn the affected enamel a dark brown, which cannot be removed. A saturated solution of zinc chloride applied once a month for six or eight months will usually prevent destruction, and the natural color will gradually return. It may take a year or so. Dry the tooth, apply the zinc chloride with a pledget of cotton, and keep it dry for a few minutes. This method has given excellent results for many years.*

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The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*To the best knowledge of this consultant, there have been no reports of tooth discoloration following the application of sodium fluoride paste as recommended for the treatment of hypersensitive dentine. Discoloration has been observed from the use of stannous fluoride, topically applied, as a means of controlling dental caries. Stannous fluoride has not been recommended for the treatment of hypersensitive dentine. The latest edition of Accepted Dental Remedies, 1958, suggests the use of equal parts of sodium fluoride, kaolin, and glycerin for the treatment of hypersensitive dentine on the cervical areas of the teeth. In this same edition, on page 189, a formula for this preparation is given. The only explannation this consultant can give is that a stannous fluoride preparation was used instead of the sodium fluoride preparation recommended or that some other ingredient besides sodium fluoride was responsible for the tooth discoloration observed.*

GLAUCOMA AND HYPOTENSIVE DRUGS

To the Editor:—*A query on glaucoma and hypotensive drugs appeared in* The Journal, *Dec. 21, 1957, page 2139. In view of the scarcity of information on this subject, as your consultant pointed out, it might be worthwhile mentioning two articles of interest in this connection. In one* (Brit. J. Ophth. 36:593, 1952; *abstracted,* J. A. M. A. 151:864 *[March 7] 1953) the author reports consistent drops in intraocular pressure*

in a small group of patients with severe hypertension who were given intramuscular injections of pentamethonium bromide. In the other (Am. J. Ophth. 43:550, 1957) *the authors describe significant falls in intraocular pressure in patients with glaucoma to whom reserpine was administered intravenously. It was suggested that the fall in intraocular pressure in normotensive eyes was related to the drop in arterial pressure. However, in eyes with elevated ocular tensions, mechanisms other than those concerned with blood pressure were excessively effective.*

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MICROMETHOD DETERMINATION OF BILIRUBIN IN ERYTHOBLASTOSIS

To the Editor:—*In* The Journal, *Aug. 24, 1957, page 1995, in Queries and Minor Notes, there is an error in the answer to the question on micromethod determination of bilirubin in erythroblastosis. The sentence "If a Coleman spectrophotometer is used, filter no. 550 should be used" is incorrect. There are not any filters used in these instruments at all. The spectrophotometers are constructed on the principle of making a spectrum (usually by means of an optical gratin), from which the beam of respective wave length can be elected. The main advantage of spectrophotometers is that a very monochromatic beam can be achieved. Thus the sentence should be: "If a Coleman spectrophotometer is used, we should set the wave length on 550 mμ.*

In an article by Mertz and West (A. M. A. Am. J. Dis. Child. 91:19, 1956) *a very quick and simple micromethod is described in which only 0.1 ml. of serum is needed. The Van den Bergh method is now going out of use, due to errors, especially in cases of hemolytic serum determinations. In the very determination of the bilirubin level in erythroblastoses, a hemolysis-free serum cannot be obtained, because the hemolysis is a fundamental characteristic of erythroblastosis.*

Docent Dr. A. Palacky
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County General Hospital
Uh. Hradiště, Czechoslovakia.

The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*An error was made; the sentence should read: "If a Coleman spectrophotometer is used, the wave length on 550 mμ is correct." It is true that the Van den Bergh test is used for the determination of direct and indirect bilirubin levels. In some cases of erythroblastosis where the serum may be hemolyzed, it is recommended that in the photometer the red filter be used because it takes out the red from the hemolyzed serum and leaves the yellow color in the serum for bilirubin determination.*

IRRITATION DURING ULTRASOUND TREATMENT

To the Editor:—*A question on superficial irritation and burning pain during treatment of ultrasonic diathermy was asked in* The Journal, *Dec. 21, 1957, page 2140. This is a common occurrence when there is improper coupling between skin and applicator in ultrasonic generators where there is no provision for reducing the power to avoid overheating of the transducer. This has occurred especially during experiments where the higher dosages are used and a portion of the body contour cannot adapt itself well to applicator surface. Should the patient complain of this, it is imperative to add more coupling medium and apply firm pressure on the applicator. The reason for the overheating and thus the superficial pain, and occasionally a burn, is the marked difference of acoustic impedance of air and the applicator surface causing almost the entire amount of ultrasonic energy to be reflected at the applicator surface—air interface.*

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METASTASIS FROM TESTICULAR TUMOR

To the Editor:—*In Queries and Minor Notes,* The Journal, *Dec. 14, 1957, page 2033, a problem concerning the treatment of metastasis from testicular tumor was presented. I believe that biopsy, if possible, should certainly be done. An article appeared in* Radiology (65:599, 1955), *describing a new chemotherapeutic agent that has been used apparently with good results, in cases of wide-spread metastases from testicular tumors.*

Dr. Joseph M. James
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Waterbury, Conn.

The above comment was referred to the consultant who answered the original query, and his reply follows:—Ed.

To the Editor.—*The article to which this letter refers mentions only one case report, the entire description being limited to a single short paragraph. It is the feeling of this consultant that chemotherapy in carcinoma is not yet sufficiently well established to suggest its use without careful control.*